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Home-based chemically-induced whitening (bleaching) of teeth in adults (Review)

Eachempati P, Kumbargere Nagraj S, Kiran Kumar Krishanappa S, Gupta P, Yaylali IE

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[Intervention Review]

Home-based chemically-induced whitening (bleaching) of teeth in adults

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ABSTRACT

Background

With the increased demand for whiter teeth, home-based bleaching products, either dentist-prescribed or over-the-counter products have been exponentially increasing in the past few decades. This is an update of a Cochrane Review first published in 2006.

Objectives

To evaluate the effects of home-based tooth whitening products with chemical bleaching action, dispensed by a dentist or over-the-counter.

Search methods

Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health's Trials Register (to 12 June 2018), the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 6) in the Cochrane Library (searched 12 June 2018), MEDLINE Ovid (1946 to 12 June 2018), and Embase Ovid (1980 to 12 June 2018). The US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (12 June 2018) and the World Health Organization International Clinical Trials Registry Platform (12 June 2018) were searched for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria

We included in our review randomised controlled trials (RCTs) which involved adults who were 18 years and above, and compared dentist-dispensed or over-the-counter tooth whitening (bleaching) products with placebo or other comparable products.

Quasi-randomised trials, combination of in-office and home-based treatments, and home-based products having physical removal of stains were excluded.

Data collection and analysis

Two review authors independently selected trials. Two pairs of review authors independently extracted data and assessed risk of bias. We estimated risk ratios (RRs) for dichotomous data, and mean differences (MDs) or standardised mean difference (SMD) for continuous data, with 95% confidence intervals (CIs). We assessed the certainty of the evidence using the GRADE approach.

Main results

We included 71 trials in the review with 26 studies (1398 participants) comparing a bleaching agent to placebo and 51 studies (2382 participants) comparing a bleaching agent to another bleaching agent. Two studies were at low overall risk of bias; two at high overall risk of bias; and the remaining 67 at unclear overall risk of bias.

The bleaching agents (carbamide peroxide (CP) gel in tray, hydrogen peroxide (HP) gel in tray, HP strips, CP paint-on gel, HP paint-on gel, sodium hexametaphosphate (SHMP) chewing gum, sodium tripolyphosphate (STPP) chewing gum, and HP mouthwash) at different concentrations with varying application times whitened teeth compared to placebo over a short time period (from 2 weeks to 6 months), however the certainty of the evidence is low to very low.

In trials comparing one bleaching agent to another, concentrations, application method and application times, and duration of use varied widely. Most of the comparisons were reported in single trials with small sample sizes and event rates and certainty of the evidence was assessed as low to very low. Therefore the evidence currently available is insufficient to draw reliable conclusions regarding the superiority of home-based bleaching compositions or any particular method of application or concentration or application time or duration of use.

Tooth sensitivity and oral irritation were the most common side effects which were more prevalent with higher concentrations of active agents though the effects were mild and transient. Tooth whitening did not have any effect on oral health-related quality of life.

Authors' conclusions

We found low to very low-certainty evidence over short time periods to support the effectiveness of home-based chemically-induced bleaching methods compared to placebo for all the outcomes tested.

We were unable to draw any conclusions regarding the superiority of home-based bleaching compositions or any particular method of application or concentration or application time or duration of use, as the overall evidence generated was of very low certainty. Well-planned RCTs need to be conducted by standardising methods of application, concentrations, application times, and duration of treatment.

PLAIN LANGUAGE SUMMARY

Home-based chemical bleaching of teeth in adults

Review question
What evidence is available regarding the different home-based chemically-induced bleaching agents in whitening teeth?

Background
There has been an increasing demand for whiter teeth. Home-based whitening products with a bleaching action have become popular and are prescribed to people by the dentist or purchased over-the-counter. A variety of whitening products are available which include hydrogen peroxide, carbamide peroxide, sodium percarbonate, sodium hexametaphosphate, sodium tripolyphosphate, and calcium peroxide. These agents are supplied in different concentrations and are used with different methods of application (gel in tray, strips, paint-on gel, chewing gum, and mouthwash), which have varying application times and duration of treatment.

Study characteristics
Authors from Cochrane Oral Health carried out this review of existing studies and the evidence is current up to 12 June 2018. We included 71 trials that involved 3780 adults who underwent tooth whitening procedures with various bleaching agents using different methods of application, length of application and duration of treatment. 26 studies compared a bleaching agent to placebo and 51 studies compared one bleaching agent to another bleaching agent.

Key results

The bleaching agents whitened teeth compared to placebo over a short time period (from 2 weeks to 6 months), however the certainty of the evidence is low to very low.

The evidence currently available is insufficient to draw reliable conclusions regarding the superiority of home-based bleaching compositions or any particular method of application or concentration or application time or duration of use.

The most common adverse events were tooth sensitivity and oral irritation, which were reported with higher concentrations of active agents, although the effects were mild and transient.

Well-planned randomised controlled trials need to be conducted by standardising methods of application, concentrations, application times and duration of treatment.

Certainty of evidence
The overall certainty of the evidence was low to very low for all comparisons. This was because most of the comparisons were reported in single trials with small sample sizes and event rates. There was an unclear risk of bias in most of the trials.

Summary of findings for the main comparison. CP gel in tray versus placebo for whitening teeth

Carbamide peroxide (CP) gel in tray compared to placebo for whitening teeth						
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** CP gel in tray **Comparison:** placebo						
Tooth whitening - assessed by the dentist						
Comparison	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with placebo	**Risk with CP gel in tray**				
10% CP gel in tray versus placebo - 6 months (higher RR indicates gel whiter)	Study population 107 per 1000	722 per 1000 (337 to 1000)	RR 6.74 (3.15 to 14.40)	109 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
5% CP gel in tray versus placebo - 2 weeks (higher shade indicates whiter)	The mean change in shade in the placebo group was 71.852	Mean difference in shade change is 4.56 units higher in the CP gel group (1.52 higher to 7.59 higher)	-	21 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP gel with desensitiser versus placebo - 2 weeks (higher shade indicates whiter)	The mean change in shade in the placebo group was 9.40	Mean difference in shade change is 4.70 units higher in the CP gel group (3.28 higher to 6.12 higher)	-	37 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP gel (lighter shade) versus placebo - 2 weeks (higher shade indicates whiter)	The mean change in shade in the placebo group was 1.40	Mean difference in shade change is 4.50 units higher in the CP gel group (4.04 higher to 4.96 higher)	-	179 teeth (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Analysis done at tooth level
10% CP gel (medium dark shade) versus placebo - 2 weeks (higher shade indicates whiter)	The mean change in shade in the placebo group was was 1.20	Mean difference in shade change is 9.30 units higher in the CP gel group (8.75 higher to 9.85 higher)	-	172 teeth (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Analysis done at tooth level

10% CP gel (dark shade) versus placebo - 2 weeks (higher shade indicates whiter)	The mean change in shade in the placebo group was 1.10	Mean difference in shade change is 10 units higher in the CP gel group (9.44 higher to 10.56 higher)	-	176 teeth (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Analysis done at tooth level
Adverse effects						
Main adverse events reported in majority of trials were mild and transient tooth sensitivity and oral irritation which occurred more in the intervention group compared to placebo						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of allocation concealment, performance and detection bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 2. HP gel in tray versus placebo for whitening teeth

Hydrogen peroxide (HP) gel in tray compared to placebo for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: HP gel in tray
Comparison: placebo

Tooth whitening - assessed by the dentist

Comparison	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with HP gel in tray				
6% HP gel versus placebo - 14 days	The mean change in shade in placebo group was 0.48	Mean difference in shade change is 3.08 units higher in the HP gel group (2.28 higher to 3.88 higher)	-	49 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

(higher shade indicates whiter)						
Adverse effects						
Not reported						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to selection, performance and detection bias.
[2]Downgraded for imprecision - single trial and low sample and event rate.

Summary of findings 3. HP strips versus placebo for whitening teeth

Hydrogen peroxide (HP) strips compared to placebo for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: HP strips
Comparison: placebo

Tooth whitening - assessed by the dentist

Comparison	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with HP strips				
10% HP strip versus placebo - day 8 (higher shade indicates whiter)	The mean change in shade in placebo group was 0.21	Mean difference in shade change is 2.24 units higher in the HP strip group (1.72 higher to 2.76 higher)	-	36 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

6% HP strip versus placebo - 2 weeks (higher shade indicates whiter)	-	Mean difference in shade change is 2.24 units higher in the HP strip group (1.83 higher to 2.66 higher)	-	195 (4 RCTs)	⊕⊕⊖⊖ LOW[1, 2]	-
10% HP strip versus placebo - 15 days (higher shade indicates whiter)	The mean change in shade in placebo group was 0.90	Mean difference in shade change is 1.93 units higher in the HP strip group (1.34 higher to 2.52 higher)	-	40 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
14% HP strip versus placebo - 3 weeks (higher shade indicates whiter)	The mean change in shade in placebo group was 1.90	Mean difference in shade change is 7.60 units higher in the HP strip group (6.18 higher to 9.02 higher)	-	28 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
6% HP strip versus placebo - 6 weeks (higher shade indicates whiter)	The mean change in shade in placebo group was 1.82	Mean difference in shade change is 2.90 units higher in the HP strip group (1.73 higher to 4.07 higher)	-	37 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
14% HP strip versus placebo - 6 weeks (higher shade indicates whiter)	The mean change in shade in placebo group was 0.45	Mean difference in shade change is 5.16 units higher in the HP strip group (4.21 higher to 6.11 higher)	-	35 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
5.3% HP strip versus placebo - 6 months (higher shade indicates whiter)	The mean change in shade in placebo group was 1.02	Mean difference in shade change is 1.21 units higher in the HP strip group (0.67 higher to 1.75 higher)	-	52 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Main adverse events reported in majority of trials were mild and transient tooth sensitivity and oral irritation which occurred more in the intervention group compared to placebo						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to selection, performance, detection bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 4. CP paint-on gel versus placebo for whitening teeth

Carbamide peroxide (CP) paint-on gel compared to placebo for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: CP paint-on gel
Comparison: placebo

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with CP paint-on				
18% CP paint-on gel versus placebo - 3 weeks (higher shade indicates whiter)	The mean shade change in the placebo group was 0.34	Mean difference in the shade change was 3.50 higher in the CP paint-on gel group (3.12 higher to 3.88 higher)	-	77 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Adverse effects

Not reported

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to selection and detection bias.
[2]Downgraded for imprecision - single trial and low sample and event rate.

Summary of findings 5. HP paint-on gel versus placebo for whitening teeth

Hydrogen peroxide (HP) paint-on gel compared to placebo for whitening teeth						
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** HP paint-on gel **Comparison:** placebo						
Tooth whitening - assessed by the dentist						
Comparisons	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with placebo	**Risk with HP paint-on**				
6% HP paint-on gel versus placebo - 2 weeks (higher shade indicates whiter)	-	SMD was 0.67 higher in HP paint-on gel group (0.19 higher to 1.14 higher)	-	148 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Main adverse events reported in majority of trials were mild and transient tooth sensitivity and oral irritation which occurred more in the intervention group compared to placebo						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to selection, performance, and detection bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 6. SHMP chewing gum versus placebo for whitening teeth

Sodium hexametaphosphate (SHMP) chewing gum compared to placebo for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: SHMP chewing gum
Comparison: placebo

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with SHMP chewing gum				
7.5% SHMP chewing gum versus placebo - 2 days (higher shade indicates whiter)	The mean shade change in placebo gum was -4.28	Mean difference in the shade change was 0.89 higher in the SHMP chewing gum group (0.77 higher to 1.01 higher)	-	37 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
5.6% SHMP chewing gum versus placebo - 3 days (higher shade indicates whiter)	The mean shade change in placebo gum was -7.27	Mean difference in the shade change was 2.60 higher in the SHMP chewing gum group (1.45 higher to 3.75 higher)	-	20 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
4% SHMP chewing gum versus placebo - 12 weeks (higher shade indicates whiter)	The mean shade change in placebo gum was -1.27	Mean difference in the shade change was 0.14 lower in the SHMP chewing gum group (0.38 lower to 0.10 higher)	-	108 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Adverse effects

Not reported

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to selection, performance, and detection bias.
[2]Downgraded for imprecision - single trial and low sample and event rate.

Summary of findings 7. STPP chewing gum versus placebo for whitening teeth

Sodium tripolyphosphate (STPP) chewing gum compared to placebo for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: STPP chewing gum
Comparison: placebo

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with STPP chewing gum				
1% STPP chewing gum versus placebo - 6 weeks (higher shade indicates whiter)	The mean shade change in placebo gum was -0.09	Mean difference in the shade change was 0.18 higher in the STPP chewing gum group (0.10 higher to 0.26 higher)	-	108 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Adverse effects

Not reported

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of allocation concealment.
[2]Downgraded for imprecision - single trial and low sample and event rate.

Summary of findings 8. HP mouthwash versus placebo for whitening teeth

Hydrogen peroxide (HP) mouthwash compared to placebo for whitening teeth						
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** HP mouthwash **Comparison:** placebo						
Tooth whitening - assessed by the dentist						
Comparisons	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with placebo	**Risk with HP mouthwash**				
1.5% HP + 0.05% HF mouthwash versus placebo - 6 months (higher OR indicates whiter)	Study population 0 per 1000	0 per 1000 (0 to 0)	OR 10.89 (5.08 to 23.35)	78 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Log of odds ratio and SE were calculated and data analyzed using generic inverse variance method
Adverse effects						
Not reported						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **F:** fluoride; **OR:** odds ratio; **RCT:** randomised controlled trial; **SE:** standard error

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to attrition bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 9. CP gel in tray versus CP gel in tray for whitening teeth

Carbamide peroxide (CP) gel in tray compared to CP gel in tray for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: CP gel in tray
Comparison: CP gel in tray

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CP gel in tray	Risk with CP gel in tray				
10% CP versus 10% CP - 2 weeks (higher RR indicates whiter)	Study population 912 per 1000	937 per 1000 (704 to 990)	RR 1.03 (0.90 to 1.18)	66 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP versus 16% CP - 2-year follow-up (higher shade indicates whiter)	The mean after intervention in 10% CP group was -81	Mean difference in shade change was 1.20 higher in 16% CP group (0.35 lower to 2.75 higher)	-	81 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
16% CP versus 16% CP + ACP - 6 months (higher shade indicates whiter)	The mean change in 16% CP group was -5.45	Mean difference in shade change was 0.78 higher in 16% CP + ACP group (0.37 higher to 1.19 higher)	-	27 (1 RCT)	⊕⊕⊖⊖ LOW[2]	-
5% CP versus 10% CP - 2 weeks (higher shade indicates whiter)	The mean after intervention for 10% CP group was -76.813	Mean difference in shade change was 0.41 higher in 5% CP group (2.17 lower to 2.98 higher)	-	21 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP versus 15% CP - 2 weeks (higher shade indicates whiter)	-	Mean difference was 2.22 higher in 15% CP group (1.29 higher to 3.15 higher)	-	25 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP versus 10% CP + KN + NaF - 2 weeks	-	Standardised mean difference was 0.32 higher in 10% CP + KN + NaF group (0.20 lower to 0.84 higher)	-	58 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Tooth whitening - reported by the patient

10% CP versus 17% CP - 3 weeks (higher shade indicates whiter)	The mean change in shade for 10% CP group was -14.10	Mean difference in patient contentment was 2.6 higher in 17% CP group (2.57 higher to 2.63 higher)	-	20 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Adverse effects

Higher concentrations of CP in tray led to more tooth sensitivity and gingival irritation. However, the symptoms were mild and transient. CP in tray with desensitiser showed significantly less sensitivity compared to the groups without the desensitiser

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

ACP: amorphous calcium phosphate; **CI:** confidence interval; **KN:** potassium nitrate; **NaF:** sodium fluoride; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of allocation concealment.
[2] Downgraded for imprecision - low sample size and event rate.

Summary of findings 10. CP gel in tray versus HP gel in tray for whitening teeth

Carbamide peroxide (CP) gel in tray compared to hydrogen peroxide (HP) gel in tray for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: CP gel in tray
Comparison: HP gel in tray

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CP gel in tray	Risk with HP gel in tray				

10% CP versus 7.5% HP - 2 weeks (higher shade indicates whiter)	The mean shade change in the CP gel in tray group was 3.40	Mean difference in shade change was 1 lower in the HP group (2.86 lower to 0.86 higher)	-	48 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
20% CP versus 9% HP - 2 weeks (higher shade indicates whiter)	The mean shade change in the CP gel in tray group was -6.97	Mean difference in shade change was 0.58 lower in the HP group (8.01 lower to 6.85 higher)	-	37 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
20% CP versus 7.5% HP - 12 days (higher shade indicates whiter)	The mean shade change in the CP gel in tray group was -2.59	Mean difference in shade change was 0.99 lower in the HP group (2.32 lower to 0.34 higher)	-	56 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
20% CP versus 7.5% HP - 12 weeks (higher shade indicates whiter)	The mean shade change in the CP gel in tray group was -2	Mean difference in shade change was 0.25 lower in the HP group (0.40 lower to 0.10 lower)	-	24 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
10% CP versus 6% HP (darker shade) - 2 weeks (higher shade indicates whiter)	The mean shade change in the CP gel in tray group was -11.10	Mean difference in shade change was 4.30 lower in the HP group (5.02 lower to 3.58 lower)	-	164 teeth (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Analysis done at tooth level
10% CP versus 6% HP (medium dark and lighter shade) - 2 weeks (higher shade indicates whiter)	-	Mean difference in shade change was 2.22 lower in the HP group (2.63 lower to 1.81 lower)	-	349 teeth (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	Analysis done at tooth level
Adverse effects						
No difference was found between HP and CP in tray groups in relation to tooth sensitivity and oral irritation						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of allocation concealment.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 11. HP strips versus CP gel in tray for whitening teeth

Hydrogen peroxide (HP) strips compared to carbamide peroxide (CP) gel in tray for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: HP strips
Comparison: CP gel in tray

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CP gel in tray	Risk with HP strips				
6% HP versus 5% CP + 5% KN - 1 week (higher shade indicates whiter)	The mean change in shade for the CP gel in tray was -1.20	Mean difference was 0.71 higher for the strip group (1.35 lower to 0.07 lower)	-	32 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
6% HP versus 10% CP - 2 weeks (higher shade indicates whiter)	-	Mean difference was 0.42 higher for the strip group (0.92 lower to 0.09 higher)	-	149 (4 RCTs)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
14% HP versus 35% CP - 30 days (higher shade indicates whiter)	The mean change in shade for the CP gel in tray was -4	Mean difference was 0.58 lower for the strip group (0.61 lower to 1.77 higher)	-	24 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
6% HP versus 10% CP - 6 weeks (higher shade indicates whiter)	The mean change in shade for the CP gel in tray was -0.90	Mean difference was 0.30 higher for the strip group (0.95 lower to 0.35 higher)	-	36 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
6.5% HP versus 15% CP - 3 months (higher shade indicates whiter)	The mean change in shade for the CP gel in tray was -8.76	Mean difference was 3.15 lower for the strip group (0.15 lower to 6.45 lower)	-	24 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
6.5% HP versus 16% CP - 21 days (higher shade indicates whiter)	The mean change in shade for the CP gel in tray was 2.10	Mean difference was 2.10 lower for the strip group (1.16 lower to 3.04 lower)	-	55 (1 RCT)	⊕⊕⊖⊖ LOW[2]	-

Adverse effects

When HP strips were compared to CP gel in tray, results were variable for adverse reactions (tooth sensitivity and oral irritation) with some trials favouring the strip group, some favouring the tray group and some showing no differences between the groups

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI)

CI: confidence interval; **KN:** potassium nitrate; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 12. HP strips versus HP gel in tray for whitening teeth

Hydrogen peroxide (HP) strips compared to HP gel in tray for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: HP strips
Comparison: HP gel in tray

Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with HP gel in tray	Risk with HP strips				
14% HP strip versus 9.5% HP gel in tray - 22 days (higher shade indicates whiter)	The mean shade change for HP gel in tray was -1.75	Mean difference was 1.40 higher for the strip group (2.35 lower to 0.45 lower)	-	29 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
5.3% HP strip versus 5% HP gel in tray - 18 months (higher shade indicates whiter)	The mean shade change for HP gel in tray was -6.35	Mean difference was 0.06 higher for the strip group (2.36 lower to 2.24 higher)	-	28 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-

Patient comfort						
5.3% HP strip versus 5% HP gel in tray	The mean patient acceptance for HP gel in tray was 2.23	Mean difference in patient acceptance was 1.27 lower for the strip group (0.13 higher to 2.41 higher)	-	28 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Tooth sensitivity and oral irritation were mild and transient and did not differ between the groups						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - single trials, low sample and event rate.

Summary of findings 13. HP strips versus HP strips (different concentrations) for whitening teeth

Hydrogen peroxide (HP) strips compared to HP strips for whitening teeth						
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** HP strips **Comparison:** HP strips						
Tooth whitening - assessed by the dentist						
Comparisons	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with 10% HP strips	**Risk with HP strips**				

6% HP versus 10% HP thin gel - 15 days (higher shade indicates whiter)	The mean shade change in 10% thin HP gel strip group was -3.03	Mean difference in 6% HP strip group was 0.68 lower (0.16 higher to 1.20 higher)	-	35 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
9.5% adhesion HP strips versus 10% HP strips - day 9 (higher shade indicates whiter)	The mean shade change in 10% HP strip group was -2.30	Mean difference in 9.5% adhesion strip group was 1.50 higher (2.33 lower to 0.67 lower)	-	29 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
When HP strips were compared to HP strips , very thin gel had lesser tooth sensitivity compared to thicker gel even though the concentration of HP was higher. Strips applied for 2 hours had greater symptoms of sensitivity compared with 30-minute group. However, these results were not significant						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance, detection and attrition bias.
[2]Downgraded for imprecision - single trials, low sample and event rate.

Summary of findings 14. CP paint-on gel versus HP strips for whitening teeth

Carbamide peroxide (CP) paint-on gel compared to hydrogen peroxide (HP) strips for whitening teeth

Patient or population: adults undergoing bleaching
Setting: home-based
Intervention: CP paint-on
Comparison: HP strips

Tooth whitening - assessed by the dentist

Comparison	Anticipated absolute effects* (95% CI)	Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments

	Risk with CP paint-on	Risk with HP strips				
18% CP paint-on gel versus 6% HP strips (higher shade indicates whiter)	-	Standardised mean difference for HP strip group was 1.50 higher (1.06 higher to 1.94 higher)	-	102 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Not reported						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - low sample size and event rate.

Summary of findings 15. HP paint-on gel versus HP strips for whitening teeth

Hydrogen peroxide (HP) paint-on gel compared to HP strips for whitening teeth					
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** HP paint-on **Comparison:** HP strips					
Tooth whitening - assessed by the dentist					
Comparisons	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with 5.9% HP paint-on	**Risk with 5.9% HP strip**				

5.9% HP paint-on versus 5.9% HP strip (higher shade indicates whiter)	-	Mean difference in 5.90% HP strip group was 2.70 higher (2.08 higher to 3.32 higher)	-	40 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Tooth whitening - reported by the patient						
5.9% HP paint-on versus 5.9% HP strip (higher shade indicates whiter)	The mean patient satisfaction for 5.90% HP paint on gel group was -4	Mean difference in patient satisfaction was 0.25 lower for 5.90% HP strip group (1.88 lower to 1.38 higher)	-	40 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	
Adverse effects						
Adverse events were mild in severity, and did not contribute to any treatment modification or early withdrawal. Slightly higher tooth hypersensitivity and gingival irritation in the strip group was found although there was no evidence of a difference between the groups						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - single trial, low sample and event rate.

Summary of findings 16. CP paint-on versus CP paint-on (different concentrations) for whitening teeth

Carbamide peroxide (CP) paint-on compared to CP paint-on for whitening teeth
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** CP paint-on **Comparison:** CP paint-on
Tooth whitening - assessed by the dentist

Comparisons	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 18% CP paint-on	Risk with CP paint-on				
18% CP paint-on 2x versus 18% CP paint-on 4x - 1 week (higher shade indicates whiter)	The mean shade change in the 18% CP paint-on 2x group was -2.79	Mean difference in shade change was 1.39 higher in 18% CP paint-on 4x group (0.50 higher to 2.28 higher)	-	69 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
18% CP paint-on versus 16.40% CP paint-on - 2 weeks (higher shade indicates whiter)	The mean shade change in the 18% CP paint-on group was 8.20	Mean difference in shade change was 0.70 lower in the 16.40% CP paint-on group (2.21 lower to 0.81 higher)	-	93 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Very mild tooth sensitivity was found in the 4 times daily application group. Both gingival and tooth sensitivity were reported to be transient and caused none of the subjects to withdraw from the study						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial; **2x:** twice; **4x:** 4 times

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - single trials, low sample and event rate.

Summary of findings 17. CP paint-on versus HP paint-on for whitening teeth

Carbamide peroxide (CP) paint-on compared to hydrogen peroxide (HP) paint-on for whitening teeth
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** CP paint-on

Comparison: HP paint-on

Tooth whitening - assessed by the dentist						
Comparison	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with CP paint-on	**Risk with HP paint-on**				
25% CP paint-on versus 8.75% HP paint-on (higher shade indicates whiter)	The mean change in shade in 25% CP paint-on group was 6.54	Mean difference in shade change was 0.16 lower in 8.75% HP paint-on group (1.39 lower to 1.07 higher)	-	59 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Not reported						

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - single trial, low sample and event rate.

Summary of findings 18. HP paint-on versus HP paint-on for whitening teeth

Hydrogen peroxide (HP) paint-on compared to HP paint-on for whitening teeth
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** HP paint-on **Comparison:** HP paint-on
Tooth whitening - assessed by the dentist

Comparison	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 6% HP paint-on	Risk with 6% HP paint-on with KF				
6% HP paint-on versus 6% HP paint-on with KF (higher shade indicates whiter)	The mean shade change in the 6% HP paint-on group was 2.70	Mean difference in shade change was 0.10 lower in 6% HP paint-on with KF (0.56 lower to 0.36 higher)	-	67 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
Tooth sensitivity was noted in both groups with no evidence of a difference						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **KF:** potassium fluoride; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection, performance and detection bias.
[2]Downgraded for imprecision - single trial, low sample and event rate.

Summary of findings 19. SPC paint-on versus CP paint-on for whitening teeth

Sodium percarbonate (SPC) paint-on compared to CP paint-on for whitening teeth
Patient or population: adults undergoing bleaching **Setting:** home-based **Intervention:** SPC paint-on **Comparison:** CP paint-on

Tooth whitening - assessed by the dentist						
Comparison	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with CP paint-on	**Risk with SPC paint-on**				

19% SPC paint-on versus 18% CP - 14 days (higher shade indicates whiter)	The mean shade change in 18% CP paint-on group was -0.55	Mean difference in shade change was 0.58 higher in the SPC paint-on group (0.95 lower to 0.21 lower)	-	38 (1 RCT)	⊕⊖⊖⊖ VERY LOW[1, 2]	-
Adverse effects						
1 subject in 19% SPC paint-on group reported oral sensitivity. All adverse events were symptomatic and mild in severity						

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded for risk of bias - unclear risk of bias due to lack of selection and detection bias.
[2]Downgraded for imprecision - single trial, low sample and event rate.

BACKGROUND

Aesthetic dentistry has received increased attention in recent years, especially because people are more concerned about the aesthetic appearance of their smile (Demarco 2009). Technological innovations in dentistry have been added due to patients' desire to improve aesthetics of their teeth, which is an important aspect of quality of life (Pinto 2014). A survey conducted in the UK revealed that 28% of adults were dissatisfied with their smile and among 3215 subjects examined, 50% had some kind of tooth discolouration (Joiner 2006). Another survey performed in the UK in 2004 suggested that the public is concerned about dental appearance in terms of tooth colours (Alkhatib 2004). Based on the survey conducted by the American Academy of Cosmetic Dentistry in 2012, discoloured, stained or yellow teeth were the main reason for an unattractive smile. The same survey reported that there was a 29% increase in patients receiving tooth whitening in a span of 1 year and was expected to increase to 45% and more in the years to come. 70% of patients who opted for bleaching were females. 75% of respondents reported the use of at-home or over-the-counter whitening products. 18% of dentists in the US recommended a home-based bleaching method (Whitening survey 2012).

With this increased demand for whiter teeth, tooth whitening products have been exponentially increasing in the past few decades. Presently, tooth whitening products are the most popularly marketed oral care products (Whitening survey 2012).

Description of the condition

Tooth discolouration can be described as any change in the colour or translucency of a tooth and can be classified based on aetiology as extrinsic or intrinsic discolourations. Extrinsic discolourations adhere to the tooth surface (superficial stains), while intrinsic discolourations are integrated in the structure of teeth (Demarco 2009). However, in some cases, both intrinsic and extrinsic discolourations may affect tooth enamel, dentine or pulp.

Extrinsic staining

This usually results from accumulation of chromatogenic substances on the external tooth surface. These include smoking, pigments in foods and beverages, and metals such as iron or copper which lead to dark, brownish discolourations. These stains are localised mainly in the pellicle and are either generated by the reaction between sugars and amino acids or acquired from the retention of exogenous chromophores in the pellicle (Viscio 2000). This reaction is called Maillard reaction or the non-enzymatic browning reaction. Most extrinsic stains can be removed by routine prophylactic procedures. With time, these stains darken and become more persistent but they are highly responsive to bleaching.

Intrinsic staining

This can result from genetic disorders such as dentinogenesis imperfecta, amelogenesis imperfecta, thalassaemia, sickle cell anaemia, antibiotics such as tetracyclines, high levels of fluoride intake, dental caries, pulpal haemorrhage, pulpal necrosis, pulp tissue remnants, root filling materials/endodontic irrigation, or amalgam restorations (Nathoo 1997; Kim 2010; Belobrov 2011; Carey 2014; Kolosowski 2014). Likewise, high fevers during the time of a tooth development may cause enamel hypoplasia that leads to banding-type discolourations on the affected tooth surface. Aging is another common cause of discolouration. Over time, dentine tends to darken due to the formation of secondary dentine and the overlying enamel becomes thinner. Intrinsic stains cannot be removed by regular prophylactic procedures. However, they can be reduced by bleaching with agents penetrating the enamel and dentine to oxidize the chromogens, in some conditions.

Description of the intervention

Tooth whitening or bleaching is a procedure most commonly employed by professionals and patients. It is considered the least invasive aesthetic treatment for improving the appearance of discoloured teeth (Pinto 2014). It may be accomplished by physical removal of the stain or a chemical reaction (bleaching) to lighten the tooth colour. The active ingredient in most chemically-induced whitening products is hydrogen peroxide (H_2O_2) which is delivered as hydrogen peroxide (HP) or carbamide peroxide (CP). CP is a stable complex, which will break down to HP and urea, once in contact with water. The basic bleaching action is due to the HP, which can be explained in three phases (Joshi 2016):

- initial phase: diffusion of HP through the inter-prismatic spaces and circulation within the tooth for 2 weeks;
- second phase: interaction of HP with organic chromophores which can be influenced by temperature, pH, light and metal cations (Kwon 2015);
- third phase: colour change through an altered tooth surface.

Bleaching action reaches an end point which is known as inherent lightness potential for that tooth (Matis 2000). Usually if there is no improvement in the shade after 6 weeks of bleaching, irrespective of the bleaching agent and concentration, then bleaching is assumed to have reached its end point (Joshi 2016).

Types of dental bleaching procedures

Tooth discolourations can be improved by several methods such as internal bleaching for non-vital teeth, or external bleaching for vital teeth (Joiner 2006) or a combination of techniques.

Internal bleaching/non-vital bleaching

It consists of walking bleach and thermocatalytic bleaching techniques and is done after endodontic treatment by the dentist and comprises of in-office techniques, which are not in the scope of this review.

External bleaching methods/vital bleaching

There are three fundamental approaches for bleaching vital teeth.

1. In-office or power bleaching (not in the scope of this review).
2. At-home or dentist-supervised bleaching.
3. Consumer-purchased or over-the-counter (OTC) products which are available in pharmacies or supermarkets without any prescription or professional monitoring.

(Other non-dental products like malic acid found in juice of green apples or do-it-yourself whitening with strawberry and baking soda were reported (Kwon 2015) but are not in the scope of this review.)

This review includes only at-home or dentist-supervised bleaching and consumer-purchased or OTC products.

Home-based bleaching methods (dentist-supervised and OTC)

A variety of peroxide compounds, including hydrogen peroxide (HP), carbamide peroxide (CP) or urea peroxide, sodium percarbonate (SPC), sodium hexametaphosphate (SHMP), sodium tripolyphosphate (STPP), and calcium peroxide have been used as active ingredients in home-based bleaching methods. These agents are supplied in different concentrations, used with varying application times and duration of treatment (Alqahtani 2014), and delivered in various forms.

Gels in trays

Dentist-supervised home-use tooth bleaching with custom trays is the most common bleaching procedure dispensed by dentists to their patients. Usually, this treatment modality consists of fabrication of a custom tray with and without reservoirs (Javaheri 2000; Caballero 2006; Baroudi 2014).

Whitening strips

These strips mainly contain hydrogen peroxide as the active agent in different concentrations. They are applied directly to the tooth surfaces and are thin flexible polyethylene strips coated with the bleaching gel. Continued research led to the development of strip-based whitening with very thin peroxide gels less than 0.20 mm in thickness (Perdigão 2004; Duschner 2006).

Disadvantages of the strip system are that it can reach only a finite number of teeth, cannot adapt well on malposed teeth, may interfere with speech patterns and can impinge on gingiva.

Paint-on gels

Paint-on gels or varnishes are barrier-free whitening products that present hydrogen or carbamide peroxide in a suspension that is brushed by an applicator over the tooth surface and which adheres to enamel. Some paint-on gels have sodium percarbonate as their active ingredient. This method has gained popularity since the consumer just needs to paint a thin layer of whitening gel on their teeth (similar to nail polish application on finger nails). The added advantage is that the users can scallop the product around the gingiva and apply it to an unlimited number of teeth, regardless of the position in the arch.

A disadvantage of this method is that lesser contact time of these agents to the tooth surface may result in reduced whitening of teeth. In addition, the applicator brush is re-used and stored in the gel product which might lead to microbial contamination. Hence, some manufacturers supply disposable cotton bud applicators for this purpose (Goldstein 1995; Carey 2014).

Whitening mouthrinses

Whitening mouthrinses prevent stains and fight plaque build-up. Generally, a low concentration of hydrogen peroxide (1.5%), sodium hexametaphosphate have been included in the formulation to protect the teeth surface from new stains (Lima 2012).

Whitening chewing gums

These are well accepted and enjoyed by many as a frequent activity among children and adults, therefore, may be a means for local drug administration into the oral cavity (Barabolak 1991). Chewing gum based products possess a number of therapeutic benefits, including increased saliva flow and removal of food debris, plaque and surface stains (Walters 2004). Baking soda (Mankodi 2001; Soparkar 2001), sodium hexametaphosphate (White 2002; Walters 2004), and sodium tripolyphosphate (Shellis 2005; Porciani 2010) have been reported as the active ingredients in chewing gums.

Whitening dentifrices

The active components of tooth whitening dentifrices include hydrogen peroxide or carbamide peroxide which break down the organic molecules of biological film (Horn 2014). Additionally, abrasives such as alumina, dicalcium phosphate dihydrate and silica are also present in the formulation to promote stain removal (Demarco 2009). Their stain removal ability is related to the large quantity of abrasives in their formulation, which remove superficial extrinsic stains. However, the toothpaste abrasiveness needs to be moderated in order to prevent excessive wear to the underlying enamel and dentine. Toothpastes containing blue covarine, a pigment, which increases the perception of tooth whiteness are available in the market as bleaching toothpastes (Dantas 2015). Whitening dentifrices with desensitizing agents (Po 2014) to reduce the adverse event of sensitivity or dentifrices with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) to remineralize the enamel have been in use (de Vasconcelos 2012).

Whitening dental floss

Whitening dental floss has been introduced to promote stain reduction around the interproximal and subgingival areas. The stain removal properties are associated with the presence of silica in the composition, which promotes a superficial surface abrasion during application in the interdental region (Demarco 2009).

Whitening dentifrices, floss and toothbrushes which involve an abrasive action are not included in this review.

All the above products are either prescribed by the dentist for use at home or purchased by the consumer over-the-counter without professional consultation. The permitted concentration of HP varies between countries.

The at-home technique offers many advantages:

- self-administration by the patient
- less chair-side time
- high degree of safety
- fewer adverse effects
- low cost.

However, there are certain disadvantages:

- results dependent on active patient compliance and diligence of use
- high dropout rates (Leonard 2003)
- excessive use by overzealous patients leads to thermal sensitivity, reported to be as high as 67% (Haywood 1992).

How the intervention might work

General mechanism of action

Hydrogen peroxide and carbamide peroxide formulations used as gels in trays/strips/paint-on gels and mouthrinses

Tooth stains consist of compounds that have colour or darker shades called chromogens. Bleaching mainly constitutes removal

of stains by chemical degradation of these chromogens. It is hypothesized that the basic chemistry of peroxide-based whitening agents is attributed to reaction of hydrogen peroxide with the chromogens. Carbamide peroxide is also an active ingredient in many whitening products. It is a stable complex which breaks down in contact with water to release hydrogen peroxide (10% CP on contact with water, gets converted to 3% HP and 7% urea).

Chromogens fall into two categories: large organic compounds that have conjugated double bonds in their chemical structure and metal containing compounds. Bleaching of the organic compounds by hydrogen peroxide involves reacting with the double bonds to oxidize the double bond.This causes the chromogen to become a lighter coloured compound. Other hypothesized mechanisms include oxidation of proteins within the tooth matrix.

Bleaching of the metallic compounds is much more difficult. There are some professional products that contain sodium hypochlorite (NaOCl) which react with the double bonds of the chromogen in much the same way as peroxide (Carey 2014).

Sodium percarbonate used in paint-on gel

19% sodium percarbonate has been developed to deliver peroxide over a sustained period without a fixed barrier. The anhydrous system has peroxide bound in a silicone polymer suspension. Applied with a brush to the dried tooth surface, the suspension is designed to form an enamel adherent substantive film that hydrates overnight to slowly release peroxide into the tooth.

Sodium hexametaphosphate used in chewing gums

This active ingredient is a high molecular weight condensed phosphate analogue which inhibits stain chromogen adsorption reducing overall extrinsic staining.

Sodium tripolyphosphate (STPP) used in chewing gums

The inhibitory action of hydroxy apatite bound STPP on adsorption of salivary proteins, makes it an effective agent for inhibiting and removing dental stain.

Why it is important to do this review

The first published version of this Cochrane Review concluded that there was evidence that whitening products work when compared with placebo/no treatment (Hasson 2006). However, all trials in that review were short term and the majority of the included studies had low methodological quality (i.e. high risk of bias). Moreover, in the past 12 years there may have been additional randomised controlled trials published, which needed to be considered in the review. Therefore, there was a need to update this review to identify new evidence from pragmatic long-term clinical trials and also to re-look at the outcomes and comparisons used in the previous version.

OBJECTIVES

To evaluate the effects of home-based tooth whitening products with chemical bleaching action, dispensed by a dentist or over-the-counter.

METHODS

Criteria for considering studies for this review

Types of studies

Inclusion criteria

- Randomised controlled clinical trials comparing dentist-dispensed or over-the-counter (OTC) tooth whitening products (with chemical, bleaching action) with placebo or other comparable products.
- Full reports (either published or obtained from the investigators) had to be available for inclusion in the review.
- The application of tooth whitening products had to be exclusively carried out at home and outcome data had to be presented for tooth whitening, irrespective of the application time.

Exclusion criteria

- Quasi-randomised trials.

Types of participants

- Home-based whitening involving adults who were 18 years old and above were included in our review regardless of gender, race, profession, geographical location or baseline tooth shade. Because of issues related to compliance and ingestion of a bleaching agent in children and young adults, we decided to include trials including adults who were 18 years old and above.
- We included participants with teeth stained because of tetracycline use and smoking.

Types of interventions

Inclusion criteria

We considered any intervention including home-based chemically-induced whitening with the following comparisons:

- comparisons of different interventions (e.g. professional monitored versus over-the-counter; over-the-counter product A versus B; professional monitored technique A versus B);
- intervention versus placebo or no treatment;
- comparisons between different concentrations;
- comparisons between different time periods of application.

Exclusion criteria

- Combination of in-office and home-based treatments were excluded.
- Home-based products having an abrasive action or physical removal of stains were excluded from the review (e.g. whitening dentifrices, whitening dental floss).

Types of outcome measures

Primary outcomes

Two primary outcomes were of interest.

1. Tooth whitening - assessed by the dentist using any relevant tool

The American Dental Association (ADA) acceptance programme guidelines for home-based tooth whitening products specify the

use of two main methods to measure tooth colour in bleaching studies:

- value-oriented shade guides (subjective measurement); and
- electronic devices/colour measurement devices (objective measurement).

Value-oriented shade guides

Traditionally, visual colour determination is used based on visual comparison of tooth with colour standards (also called shade guides). The most common shade guides are Vitapan classical and its derivatives like Vitapan 3D master, tooth guide, bleached guide and linear guide. Ordinal scale ranging from 1 to 16 has been suggested by the manufacturer with 1 representing the lightest shade and 16 representing the darker shade. However, some authors considered 1 as the darkest and 16 as the lighter shade. Some studies reported a scale below 1 and beyond 16 when the tooth shade was lighter than the lightest shade tab and darker than the darkest shade.

Trubyte Bioform shade guide has also been used by some authors using a scale from 1 to 24.

Electronic devices/colour measurement devices

Instruments for clinical shade matching encompass spectrophotometers, colorimeters and imaging systems. They provide a more objective measurement of whiteness compared to shade guides. For instrumental colour assessment of teeth the issue of suitable metric that corresponds to perpetual whiteness is important. Colourimeters, spectrophotometers, spectroradiometer and camera systems can allow computation of CIExyz or CIEL*a*b* values described by commission international deLE clariage (CIE 1978) an international standard for three dimensional colour space.

Using a calibration standard, red-green-blue values are determined and converted to L* a* b* values where L* represents the degree of lightness and b* represents degree of yellowness. Tooth whitening is characterised by negative or decreased b* values (reduction in yellowness) and positive or increased L* values (increased lightness). A composite colour W is used by some and derived from individual L* a* b* changes from baseline values. Some clinicians use E* which indicates composite colour change irrespective of the direction of change.

In our review we considered the composite score represented by W* or E* values wherever provided. In the absence of both, the value of L* is considered as it indicates a positive change towards increased lightness.

2. Tooth whitening - reported by the patient using any relevant tool

Improvement in tooth whitening as reported by the patient using any tool was considered in this review. Some authors reported visual analogue scale (VAS) from 0 to 10 to record patient acceptance with 0 indicating best acceptance and 10 indicating no acceptance, while some others used the scale where 0 represents least satisfaction and 10 represents most satisfaction.

Other scores used were on an ordinal scale of 0 to 3 where 0 = no improvement in whiteness, 1 and 2 = moderate improvement, and 3 = improvement. In such cases, we combined 1, 2, and 3 as improvement in shade and counted them as events.

Secondary outcomes

1. Patient satisfaction or acceptability of the tooth whitening procedure (patient comfort).
2. Adverse effects: any side effects reported due to the bleaching procedure were considered in this review and described qualitatively.
3. Oral health-related quality of life.

Search methods for identification of studies

Electronic searches

Cochrane Oral Health's Information Specialist conducted systematic searches in the following databases for randomised controlled trials and controlled clinical trials. There were no language, publication year or publication status restrictions:

- Cochrane Oral Health's Trials Register (searched 12 June 2018) (Appendix 1);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 6) in the Cochrane Library (searched 12 June 2018) (Appendix 2);
- MEDLINE Ovid (1946 to 12 June 2018) (Appendix 3);
- Embase Ovid (1980 to 12 June 2018) (Appendix 4).

Subject strategies were modelled on the search strategy designed for MEDLINE Ovid. Where appropriate, they were combined with subject strategy adaptations of the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6 (Lefebvre 2011).

Searching other resources

The following trial registries were searched for ongoing studies:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov; searched 12 June 2018) (Appendix 5);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; searched 12 June 2018) (Appendix 6).

We searched the reference lists of included studies and relevant systematic reviews for further studies.

We did not perform a separate search for adverse effects of interventions used, we considered adverse effects described in included studies only.

Data collection and analysis

Selection of studies

Two review authors (Eachempati Prashanti (EP), Salian Kiran (SK)) independently screened the titles and abstracts from the electronic searches to identify potentially eligible studies. The search was designed to be sensitive and include controlled clinical trials, these were filtered out early in the selection process if they were not randomised. We obtained full-text copies of all potentially eligible studies and two pairs of review authors (EP and Ibrahim Ethem (IE), SK and Puneet Gupta (PG)) further evaluated in detail the studies for inclusion. We recorded the reasons why studies did not meet the inclusion criteria in the 'Characteristics of excluded

studies' table. We resolved any disagreements by discussion. When resolution was not possible, we consulted the arbiter (Sumanth Kumbargere Nagraj (SKN)). Articles in languages other than English were assessed by their abstracts where possible and if they appeared to be potentially eligible, we obtained and translated the full-text article.

Data extraction and management

Two pairs of review authors (EP and IE, SK and PG) extracted the data independently, using a data extraction form specifically designed for this Cochrane Review. We resolved any disagreements by discussion. The two review authors independently checked data extraction forms obtained from translators and cross checked any doubtful aspects using Google translator. We entered all study details in the 'Characteristics of included studies' table in Review Manager 5 software (Review Manager 2014). We recorded the following details for each included trial.

- Publication details like year of publication and language.
- Demographic details of the report.
- Inclusion and exclusion criteria.
- Sample size.
- Method of randomisation.
- Allocation concealment.
- Blinding.
- Type of trial.
- Method of assessing the outcome, and dropouts if any.
- Type of intervention.
- Details of the outcome reported.
- Duration of follow-up.
- Results of the intervention.
- Funding details.
- Details about trials registration.
- For obtaining additional data and clarifications, we contacted the authors of the included and excluded trials via email.

Assessment of risk of bias in included studies

We independently assessed the risk of bias in the included trials for seven domains: sequence generation; allocation concealment; performance bias and detection bias; incomplete outcome data; selective outcome reporting; and other biases. For each of these components, we assigned a judgement regarding the risk of bias as either 'high', 'low' or 'unclear', based on guidance in section 8.5.d of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We contacted the trial authors if details were missing in the publications or were unclear. We resolved disagreements through consensus. We recorded our judgements and justifications in 'Risk of bias' tables for each included study and generated a 'Risk of bias' summary figure. We used these judgements while grading of the overall quality of evidence for outcomes in the 'Summary of findings' tables for each comparison.

We summarised the risk of bias according to Higgins 2011 as follows:

Risk of bias	Interpretation	In outcome	In included studies
Low	Plausible bias unlikely to seriously alter the results	Low risk of bias for all key domains	Most information is from studies at low risk of bias
Unclear	Plausible bias that raises some doubt about the results	Unclear risk of bias for one or more key domains	Most information is from studies at low or unclear risk of bias
High	Plausible bias that seriously weakens confidence in the results	High risk of bias for one or more key domains	The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results

Measures of treatment effect

For dichotomous data, we used risk ratios (RRs), and for continuous data, we assessed the mean difference (MD) and presented results with 95% confidence intervals (CIs). For continuous data using different scales to measure the same primary outcome (improvement in tooth shade), we used the standardised mean difference (SMD). Change score and final score were combined in meta-analysis according to Higgins 2011 section 7.7.3.1. When multiple time points were given, longest follow-up time was considered (Higgins 2011, section 9.3.4).

Unit of analysis issues

For parallel-group and cluster-randomised studies, we used the individual as the unit of analysis. If clustered data were provided, we planned to adjust the standard errors of the estimates to take clustering into account (as outlined in section 16.3.4 of the *Cochrane Handbook for Systemic Reviews of Interventions* (Higgins 2011)). For split-mouth studies, we used the quadrant of the mouth within an individual as a unit of analysis. For studies that have used a split-mouth design but reported data as a parallel-group study, we calculated the odds ratios using the Becker-Balagtas method, as outlined in Curtin 2002, using Stata software.

Dealing with missing data

We attempted to obtain missing data by contacting trial authors. If both mean and standard deviation were reported as graphs, we derived the data from the graphs by magnifying them and approximating the measures of mean and standard deviation. When mean and standard error (SE) were given, we calculated the standard deviation (SD) as given in Higgins 2011, section 7.7.3.3. When adjusted mean was given, we considered it in the analysis (Higgins 2011, section 9.2.3.2). When median and inter quartile

range were given we used the data to calculate mean and SD. When mean and P value were given, SD was calculated.

When data were presented as median (skewed data), we qualitatively described the results in the review.

Assessment of heterogeneity

We assessed heterogeneity by examining the forest plot to check for overlapping CIs, using the Chi^2 test for heterogeneity with a 10% level of significance to detect inconsistency in study results that were not due to random error (chance), and the I^2 statistic to denote the percentage of inconsistency in results due to inter-trial variability that exceeded chance. We used the guidance given by the *Cochrane Handbook for Systematic Reviews of Interventions* to interpret the I^2 statistic: 0% to 40% as possibly insignificant, 30% to 60% as moderate heterogeneity, 50% to 90% as possibly substantial, and 75% to 100% as considerable heterogeneity depending on two factors: 1. inconsistency in results was due to differences in the direction of effect estimates between trials rather than due to differences in the magnitude of effect estimates favouring an intervention; 2. based on the strength of the evidence for heterogeneity from the P value for the Chi^2 test for heterogeneity (Deeks 2011).

Assessment of reporting biases

We tested for publication bias using funnel plots and a formal test investigation of the degree of asymmetry using the method proposed by Egger 1997 wherever possible.

Data synthesis

We analysed the data using Review Manager 5 software (Review Manager 2014). We combined data available from trials with similar comparisons (same concentration and duration of application) and outcomes in the meta-analysis. We used standardised mean differences to combine continuous data as some trials used different scales. We used the random-effects model in the meta-analysis. If data were presented as adjusted mean and SE, we calculated SD from SE and considered the adjusted mean for analysis. If data were described in the form of ordinal outcomes, we converted the scale into dichotomous data by combining relevant adjacent categories and analysed using risk ratios and 95% CI. When data were presented as odds ratios, log (odds ratio) was calculated based on the odds ratios and 95% CI given in the trial and the generic inverse variance method was applied. We calculated mean difference and standard error in split-mouth and cross-over trials and analysed the data using the generic inverse variance method.

Subgroup analysis and investigation of heterogeneity

We conducted subgroup analyses where there was heterogeneity.

To identify the reasons for clinical or methodological heterogeneity in meta-analyses, we carried out subgroup analyses, based on.

Population

- Age group of the patient.
- Baseline tooth shade.

Method

- Different concentrations.
- Varying application times and duration of treatment.

Outcome measures

- Subjective measurement involving shade guide.
- Objective measurements using electronic devices/instrument.

Sensitivity analysis

A sensitivity analysis is a repeat of the primary analysis or meta-analysis, substituting alternative decisions or ranges of values for decisions that were arbitrary or unclear. It involves undertaking the meta-analysis twice: first, including all studies and second, only including those that are definitely known to be eligible. Wherever feasible we did sensitivity analyses to assess the robustness of our findings by excluding data from trials at high risk and at unclear risk of bias.

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to interpret findings (Schünemann 2011). We used GRADEpro GDT 2015 (GRADEpro GDT 2015) and imported data from Review Manager 5 (Review Manager 2014) to create 'Summary of findings' tables for the comparisons included in this review. The tables provide information concerning the overall certainty of the evidence at the outcome level, the magnitude of effect of the intervention examined and the sum of available data on the primary and secondary outcomes. The GRADE approach (Schünemann 2011) considers 'certainty' to be a judgement of the extent to which we can be confident that the estimates of effect are correct. Evidence from randomised controlled studies is initially graded as high and downgraded on each of five domains after full consideration of risk of bias, indirectness, imprecision, inconsistency and publication bias. A GRADE certainty level of 'high' reflects confidence that the true effect lies close to that of the estimate of the effect for an outcome. A judgement of 'moderate' certainty indicates that the true effect is likely to be close to the estimate of the effect, but acknowledges the possibility that it could be substantially different. 'Low' and 'very low' certainty evidence limit our confidence in the effect estimate (Balshem 2011).

RESULTS

Description of studies

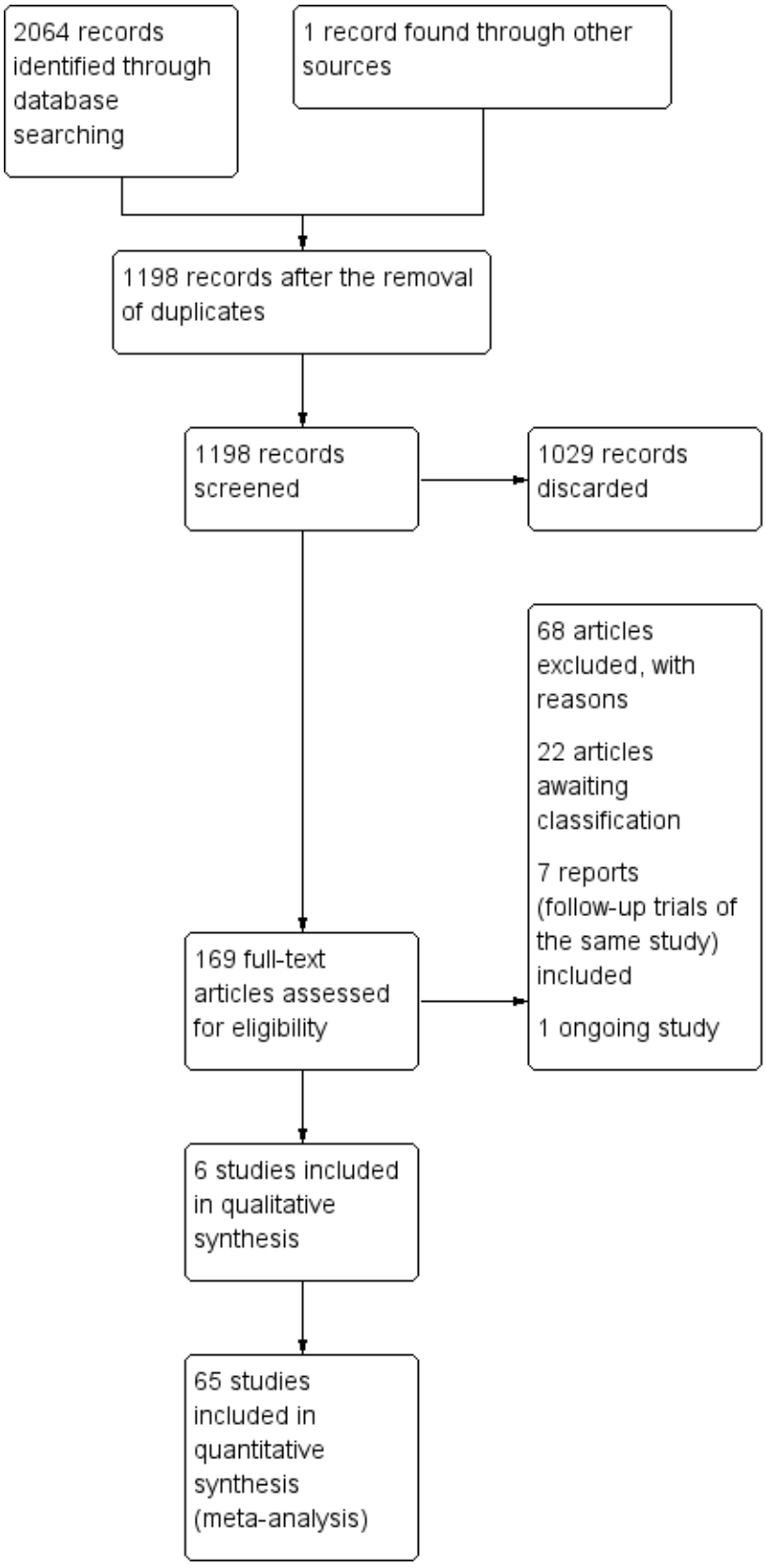
See Characteristics of included studies; Characteristics of excluded studies; and Characteristics of studies awaiting classification.

Results of the search

We included 71 trials (78 reports) in the review. (If the same study (one population) was separated into multiple reports we included the primary study and considered the rest as reports as per Higgins 2011.)

See Figure 1 for the selection process of search results.

Figure 1. Study flow diagram.



Included studies

See Characteristics of included studies for further details.

Characteristics of trial settings and investigators

Seventy studies were in the English language, one was in German (Auschill 2007).

The countries of origin for the included studies were.

- Forty-two from the USA (Kowitz 1994; Nathoo 1994; Russell 1996; Matis 1998; Cibirka 1999; Gerlach 2000; Kihn 2000; Kugel 2000; Matis 2000; Mokhlis 2000; Nathoo 2001; Gerlach 2002; Gerlach 2002a; Gerlach 2002b; Karpinia 2002; Kugel 2002; Nathoo 2002; Barlow 2003; Gerlach 2003; Li 2003; Myers 2003; Nathoo 2003; Biesbrock 2004; Garcia-Godoy 2004; Gerlach 2004; Gerlach 2004e; Hasturk 2004; Li 2004; Swift 2004; Cronin 2005; Gerlach 2005; Giniger 2005; Shahidi 2005; Matis 2006; Delgado 2007; Browning 2008; Gallo 2009; Papas 2009; Swift 2009; Bruhn 2012; Costa 2012; Oliveira 2013).
- Three trials were from Brazil (Mederios 2008; Meireles 2010; Kose 2011); five from Germany (Auschill 2007; Bizhang 2007; Krause 2008; Ziebolz 2008; Auschill 2012); four from Italy (Porciani 2006; Ferrari 2007; Porciani 2010; Navarra 2014); four from the UK (Brunton 2004; Collins 2004a; Walters 2004; Mohan 2008); three from Spain (Alonso 2006; Berga-Caballero 2006; Alonso 2014); two from Switzerland (Hannig 2007; Ziebolz 2007); two from Hong Kong (Wong 2004; Botelho 2017); one from China (Xu 2007); two from Turkey (Turkun 2010; Aka 2017); one from Japan (Tsubura 2005); one from Canada (Tam 2001); and one from Ireland (Hyland 2015).
- Sixty-one trials were parallel-design trials and seven were split-mouth (Matis 2000; Mokhlis 2000; Tsubura 2005; Alonso 2006; Matis 2006; Auschill 2007; Costa 2012); and three had a cross-over design (Biesbrock 2004; Walters 2004; Porciani 2006).
- Twelve of the included trials had more than two groups for comparison. One trial had five groups (Browning 2008). Two trials, Alonso 2014 and Gerlach 2000, had four groups. The remaining nine trials had three groups for comparison (Li 2003; Li 2004; Wong 2004; Matis 2006; Bizhang 2007; Xu 2007; Krause 2008; Hyland 2015; Aka 2017). Seven trials included placebo in their comparisons (Wong 2004; Bizhang 2007; Xu 2007; Browning 2008; Krause 2008; Hyland 2015; Aka 2017). We included these seven trials separately in both the analysis testing bleaching agent versus placebo and bleaching agent versus bleaching agent. See Additional Table 1 for details.
- Out of the 71 trials, 54 provided grant information and out of these one was government funded (Navarra 2014). 53 were funded by a pharmaceutical company (Nathoo 1994; Cibirka 1999; Gerlach 2000; Kihn 2000; Kugel 2000; Matis 2000; Mokhlis 2000; Nathoo 2001; Gerlach 2002; Gerlach 2002a; Gerlach 2002b; Karpinia 2002; Kugel 2002; Nathoo 2002; Barlow 2003; Gerlach 2003; Li 2003; Myers 2003; Nathoo 2003; Biesbrock 2004; Brunton 2004; Collins 2004a; Garcia-Godoy 2004; Gerlach 2004; Gerlach 2004e; Hasturk 2004; Li 2004; Swift 2004; Walters 2004; Wong 2004; Cronin 2005; Gerlach 2005; Giniger 2005; Shahidi 2005; Tsubura 2005; Matis 2006; Porciani 2006; Bizhang 2007; Delgado 2007; Ferrari 2007; Hannig 2007; Xu 2007; Ziebolz 2007; Ziebolz 2008; Gallo 2009; Papas 2009; Swift 2009; Porciani 2010; Kose 2011; Auschill 2012; Costa 2012; Oliveira 2013; Hyland 2015).
- All the trials were carried out in a single centre.

Characteristics of participants

Forty-seven trials reported on both genders. The remaining 24 trials did not report on distribution of gender (Kowitz 1994; Nathoo 1994; Matis 1998; Cibirka 1999; Kihn 2000; Mokhlis 2000; Nathoo 2001; Nathoo 2002; Gerlach 2003; Myers 2003; Brunton 2004; Garcia-Godoy 2004; Walters 2004; Berga-Caballero 2006; Auschill 2007; Browning 2008; Krause 2008; Gallo 2009; Turkun 2010; Kose 2011; Bruhn 2012; Alonso 2014; Navarra 2014; Hyland 2015). The minimum age included in a study was 18 years and the maximum age included in a study was 79 years (Russell 1996). The minimum sample size was six (Berga-Caballero 2006) and the maximum sample size was 117 (Collins 2004a) with a median value of 58.

Thirty-one trials reported on the minimum baseline shade for inclusion in the trial. Twelve reported A2 as the baseline shade (Kugel 2000; Karpinia 2002; Gerlach 2003; Garcia-Godoy 2004; Wong 2004; Cronin 2005; Hannig 2007; Ziebolz 2007; Ziebolz 2008; Papas 2009; Kose 2011; Oliveira 2013), 14 reported A3 as the baseline shade (Nathoo 1994; Kihn 2000; Nathoo 2001; Nathoo 2002; Nathoo 2003; Li 2003; Brunton 2004; Li 2004; Giniger 2005; Auschill 2007; Delgado 2007; Browning 2008; Mohan 2008; Auschill 2012), and three reported C1 (Matis 2006; Meireles 2010; Turkun 2010) based on Vita shade guide. Two studies used Trubyte shade guide; one used B85 as the baseline shade (Mokhlis 2000) while B65 was used in the other (Gallo 2009).

Two trials compared the effects of bleaching agent on participants with tetracycline stains (Kugel 2002; Matis 2006). One trial discussed the effect of dietary habits of participants on tooth whitening (Meireles 2010). One trial compared the effect of tooth whitening between smokers and non-smokers (Porciani 2006).

Characteristics of interventions

We divided the 71 trials included in our review into two categories.

1. Bleaching agent versus placebo

Twenty-six trials were included in this group. Among the 26 studies, the following comparisons were identified.

- Six trials comparing carbamide peroxide (CP) gel in tray versus placebo.
- Two trials comparing hydrogen peroxide (HP) gel in tray versus placebo.
- Ten trials comparing HP strips versus placebo.
- One trial comparing CP paint-on gel versus placebo.
- Two trials comparing HP paint-on gel versus placebo.
- Three trials comparing sodium hexametaphosphate (SHMP) chewing gum versus placebo.
- One trial comparing sodium tripolyphosphate (STPP) chewing gum versus placebo.
- One trial comparing HP mouthwash versus placebo.

1a. CP gel in tray versus placebo

Six trials were included in this comparison.

Hyland 2015, a three-arm study compared 10% CP and 5% CP applied 2 hours a day for 2 weeks to the placebo gel. The CP formulation in this trial contained sodium tripolyphosphate. We compared 5% CP to placebo gel.

Browning 2008 used five interventions in his multiarm study. We compared 10% CP + 0.5% potassium nitrate (KNO3) + 0.25% sodium fluoride (NaF) to a placebo gel, applied for 11 weeks.

A three-arm trial conducted by Aka 2017 used 6% HP, 10% CP and placebo. Analysis in this trial was done at tooth level. The study authors divided the groups based on the tooth shade as light, medium dark and dark. 10% CP gel was compared to placebo in our meta-analysis, which was applied for 8 hours to 10 hours daily for 14 days. For the control group, no bleaching agent was applied.

Russell 1996 and Matis 1998 used 10% CP and used it overnight for 2 weeks with a follow-up of 6 months.

Mederios 2008 used 10% CP overnight for 3 weeks.

1b. HP gel in tray versus placebo

Mohan 2008 and Myers 2003 studied the effect of 6% and 3% HP gel respectively which was applied twice daily for 14 days.

1c. HP strips versus placebo

Ten trials, studied the effect of HP strips versus placebo. All trials included HP strips with varying concentrations.

Gerlach 2004e used 10% HP, twice a day for 30 minutes for 1 week and 2 weeks respectively.

6% HP was used twice a day for 30 minutes in one multiarm trial Bizhang 2007.

Kugel 2000 used 5.3% HP, twice daily for 30 minutes each time for 2 weeks.

6% HP was used twice a day for 30 minutes in Swift 2009 for 2 weeks and 6 weeks.

Wong 2004 a multiarm trial, compared 6% HP strip, 18% CP paint-on gel and placebo. Data for 6% HP strip versus placebo were used in this meta-analysis. Strips were used twice a day for 30 minutes, for 14 days.

Papas 2009 used 10% HP, twice a day for 30 minutes for 1 week and 2 weeks.

Swift 2004 and Garcia-Godoy 2004 compared 14% HP strips applied twice daily for 30 minutes for 3 weeks and 6 weeks respectively.

Gerlach 2002 used 5.3% HP, twice daily for 30 minutes each time for 2 weeks with a follow-up of 6 months.

Bruhn 2012 used a HP gel twice a day for 3 weeks and reported on patient-reported satisfaction and oral health-related quality of life.

1d. CP paint-on gel versus placebo

One trial Nathoo 2002 compared the effect of CP paint-on gel with placebo.

Nathoo 2002 studied 18% CP versus placebo gel, which was applied immediately after brushing and subjects were instructed to keep their mouth open for 30 seconds after application. They refrained from eating and drinking for 30 minutes after application.

1e. HP paint-on gel versus placebo

Two trials compared the effect of HP paint-on gel with control gel.

Xu 2007, a multiarm trial, and Collins 2004a compared 6% and 5.9% HP gel applied twice daily for 2 weeks respectively. Collins also evaluated colour change at 1 week.

1f. SHMP chewing gum versus placebo

Three trials compared SHMP chewing gum to placebo.

Biesbrock 2004, a cross-over study used 7.5% SHMP on 19 subjects each (period A) and 18 subjects each (period B) for 5 minutes daily for 2 days followed by 60 seconds rinse with tea. This was repeated approximately 8 times a day. Outcomes looked into were stain prevention and removal. Placebo group were given a negative control chewing gum.

Porciani 2006 was another cross-over study among smokers and non-smokers, using 4% SHMP on 54 subjects each in placebo and experimental groups. The subjects chewed chewing gum 4 times a day for 12 weeks. Placebo group received no gum.

Walters 2004 compared 5.6% SHMP to a negative control chewing gum in a 3-day cross-over trial separated by a 10-day wash out period including 10 subjects in each group.

1g. STPP chewing gum versus placebo

Sodium tripolyphosphate was used in a study by Porciani 2010, including smokers and habitual tea users in each group. They were asked to chew the gum 3 times a day for 10 minutes for 6 weeks and compared to the placebo group who received a control chewing gum.

1h. HP mouthwash versus placebo

One trial (Hasturk 2004) compared 1.5% fluoridated HP-based mouthrinse to placebo. Mouthrinse was used twice daily for 30 seconds for 6 months.

2. Bleaching agent versus bleaching agent

Fifty-one trials were included in this group among which six are multiarm trials which were also included in the comparison of bleaching agent versus placebo.

Among these, the following comparisons were made.

- Eighteen trials compared CP tray versus CP tray.
- Seven trials compared CP tray versus HP tray.
- Ten trials compared HP strips versus CP tray.
- Two trials compared HP strips versus HP tray.
- Two trials compared HP strips versus HP strips.
- One trial compared HP strip versus HP mouthwash.
- Two trials compared CP paint-on versus HP strip.
- Two trials compared HP paint-on versus HP strip.
- One trial compared SPC paint-on versus HP strip.
- Two trials compared CP paint-on versus CP paint-on.
- One trial compared CP paint-on versus HP paint-on.
- One trial compared HP paint-on versus HP paint-on.
- One trial compared sodium percarbonate (SPC) paint-on versus CP paint-on.
- One trials compared SPC paint-on versus HP paint-on.

2a. CP tray versus CP tray

A total of 18 trials are included comparing CP in a tray versus CP in a tray.

Nathoo 2001 used an overnight application of 5% and 10% CP (6 to 8 hours per day) for 1 week. Hyland 2015 used the same concentrations of bleaching agent for 2 hours daily for 2 weeks.

Four trials (Kowitz 1994; Nathoo 1994; Cibirka 1999; Tsubura 2005) reported on the effect of 10% CP of different brands. Tsubura 2005 and Cibirka 1999 used the gel in tray overnight for 2 weeks while Kowitz 1994 used it for 3 hours or more for 2 weeks. Nathoo 1994 applied the gel twice daily for 30 minutes, for a duration of 2 weeks.

Turkun 2010 reported on effects of 10% CP and 28% CP with an application time of 8 hours overnight and 20 minutes per day over a 2-week period.

Meireles 2010 had 46 and 45 subjects in experimental and control groups respectively and applied the whitening agents 2 hours a day for 2 weeks. He followed the same regimen for 3 weeks with 45 and 44 participants in 10% and 16% CP groups respectively. He did a follow-up study including 45 and 44 participants for 1 year and 42 and 39 participants for 2 years respectively, following the same application protocol.

Gallo 2009 reported a trial of 10 days duration with 30% CP with and without potassium nitrate. The application time was 1 hour per day.

Kose 2011 reported the effect of bleaching with 16% CP with and without potassium nitrate and sodium fluoride. The bleaching was done for 2 weeks with 6 hours application time.

Giniger 2005 is a 5-year follow-up trial comparing the effect of 16% CP (n = 13) versus 16% CP with amorphous calcium phosphate (n = 14). The application time was 3 hours per day over 2-week period.

Matis 2006 is a follow-up trial for 180 days continued from a split-mouth trial with 40 and 39 participants in experimental and control groups on tetracycline stained teeth with overnight application using 10% CP and 15% CP over 6 months.

Krause 2008 conducted a trial on 10% CP and 17% CP with 2 hours a day application over a period of 2 weeks.

Matis 2000 and Kihn 2000 reported the effect of overnight application of 10% CP and 16% CP for 2 weeks.

Two trials, Navarra 2014 (n = 10 per group) and Browning 2008 (n = 19 per group), reported on the effect of 10% CP with and without potassium nitrate and sodium fluoride applied overnight for 2 weeks.

Tam 2001 reported a trial with 10% CP and 10% CP without potassium nitrate with overnight application time for 2 weeks.

2b. CP tray versus HP tray

Ziebolz 2007 studied the effect of 20% CP versus 7.5% HP. He used the bleaching gel for 4 hours a day for 20% CP group and 30 minutes a day for 7.5% HP group for 12 days. Mokhlis 2000 used the same concentration but applied the gel twice daily for an hour over a period of 12 weeks.

Alonso 2014 reported a 2-week trial with an application time of 1 hour per day using 10% CP and 7.5% HP.

Delgado 2007 reported on application time of 30 minutes per day over 2 weeks for 20% CP and 9% HP.

Aka 2017 reported a multiarm trial at tooth level, comparing 10% CP and 6% HP. The application time was 8 hours to 10 hours per day over 2 weeks for CP group.

Berga-Caballero 2006 reported a trial with 3.5% HP and 10% CP. The application time was 3 hours daily for 24 days for 3.5% HP group and 2 hours daily for 28 days in 10% CP group.

Alonso 2006 conducted a split-mouth study on the effect of 3.5% HP and 5% potassium nitrate over 10% CP for 4 weeks. The application time was 3 hours per day.

2c. HP strips versus CP tray

Ten trials compared HP strips to CP gel in tray in varying concentrations and application times.

Gerlach 2002b used 5% CP gel with 5% potassium nitrate in tray and compared it to 6% HP strips used for 30 minutes, twice daily for 7 days.

Gerlach 2000 a multiarm trial; Gerlach 2002a; Hannig 2007; and Karpinia 2002 compared 10% CP gel in tray versus 5.3% or 6% or 6.5% HP strips for 2 weeks. Gerlach 2002b applied the strips twice daily for 30 minutes and gel in tray for 2 hours a day, both for a duration of 2 weeks. Gerlach 2002a applied strips twice a day for 1 hour and the tray for 2 hours once daily for 2 weeks. Hannig 2007 followed the same application protocol for strips as mentioned above, however, the tray was used once daily for 1 hour over 2 weeks. Karpinia 2002 applied whitening strips for 30 minutes, twice daily and whitening gel in tray for 2 hours daily.

Costa 2012 compared 35% CP gel in tray to 14% HP strips in a split-mouth trial. Both interventions were applied simultaneously for 30 minutes, twice a day for 2 weeks and the application times were separated by 3 hours.

Ferrari 2007 used 6% HP versus 10% CP for 6 weeks. He applied the strips for 30 minutes, twice daily and gel in tray for 2 hours daily.

Kugel 2002 also followed the same regimen as Ferrari 2007 for a duration of 2 months.

Botelho 2017 used 6.5% HP strips versus 16% CP in tray with 13 and 11 participants allocated to each group respectively. The subjects wore tray with the gel for up to 2 hours or overnight during the 3-month trial. Strip group applied the strips onto the labial surfaces of the teeth twice daily for 30 minutes for 3 months.

Li 2003 a multiarm trial compared 6.5% HP strips to 7.5% HP in tray and 16% CP in tray. Strips were applied twice a day for 30 minutes and tray was used overnight, both for 21 days.

2d. HP strips versus HP tray

Two trials compared HP strips to HP gel in tray.

Gerlach 2004 compared 14% HP strips used for 21 days and 9.5% HP in custom tray used for 9 days. Both the groups applied the bleaching agent twice a day for 30 minutes.

Auschill 2012 studied 5% HP in tray and 5.3% HP strips for 30 minutes, twice daily for 14 consecutive days.

2e. HP strip versus HP strip

Oliveira 2013 compared 9.5% high adhesion HP strips to marketed 10% control strip for 8 days. 9.5% HP strips were applied for 2 hours once daily and control strips were applied for 30 minutes once a day.

Shahidi 2005 studied 10% HP strip with very thin 6% HP gel (0.12 mm strip) versus 6% HP gel (0.2 mm) applied for 30 minutes, twice daily for 14 days.

2f. HP strip versus HP mouthwash

One trial (Gerlach 2005) compared two HP tooth whitening systems including 2% HP pre-rinse and 10% HP strips. Pre-rinse group was instructed to rinse twice daily with 15 ml solution for 60 seconds before brushing. The strip group were specified twice daily application for 30 minutes.

2g. CP paint-on gel versus HP strip

Two trials compared HP strips to CP paint-on gel (Wong 2004; Cronin 2005).

Both trials compared 6% HP strips to 18% CP paint-on gel. In both trials strips were used twice daily for 2 weeks. Paint-on was used twice daily for 30 minutes for 2 weeks in Cronin 2005 and 15 minutes in Wong 2004.

2h. HP paint-on gel versus HP strip

Two trials compared 5.9% or 6% HP strips to 5.9% HP paint-on gel (Auschill 2007; Xu 2007). In Xu 2007 a multiarm trial, both the groups applied the bleaching agent twice daily for 1 week. Auschill 2007 used strips twice daily for 30 minutes and paint-on gel twice daily for 15 minutes.

2i. SPC paint-on versus HP strip

One trial compared HP strips to sodium percarbonate (Bizhang 2007).

Bizhang 2007 compared 6% HP strips to 19% SPC. Strips were instructed to be applied twice daily for 30 minutes over a 14-day period. Paint-on gel was applied to the facial surfaces of the teeth for 14 days.

2j. CP paint-on versus CP paint-on

Two trials were included in this comparison.

Li 2004 a multiarm trial with 120 participants balanced equally into three groups, used 18% CP with different application times (twice 2x, thrice 3x, 4 times 4x per day). In the 2x group, no air drying was used and participants were asked not to eat and drink for 15 minutes after the gel was applied. In the 4x group, 30 seconds air drying and 30 minutes refraining from eating and drinking was advocated.

Brunton 2004 compared 18% CP gel and 16.4% CP gel, applied twice a day for 30 seconds each for 2 weeks. Subjects were asked to refrain from eating and drinking for 30 minutes.

2k. CP paint-on versus HP paint-on

One trial (Nathoo 2003) compared 8.7% HP versus 25% CP, where a thin layer of gel was applied one tooth at a time and subjects were instructed not to rinse, eat or drink for 15 minutes. This was repeated 3 times a day for 2 weeks.

2l. HP paint-on versus HP paint-on

One trial (Ziebolz 2008) studied 6% HP after potassium fluoride application versus 6% HP without desensitiser application. Application was done twice a day for 10 minutes for 7 days.

2m. SPC paint-on versus CP paint-on

Barlow 2003 compared 19% SPC and 18% CP gel twice a day for 2 weeks.

2n. SPC paint-on versus HP paint-on

Gerlach 2003 compared 19% SPC and 8.7% HP. Both groups advocated application of a thin layer of gel after drying the tooth at night. They were instructed not to eat or drink after application and to brush normally the next morning.

Outcomes reported in the trials

Primary outcomes

Sixty-nine trials studied improvement in tooth whitening as assessed by the dentist using any relevant scale. 11 trials reported improvement in tooth whitening based on patient's satisfaction levels (Kowitz 1994; Tam 2001; Wong 2004; Matis 2006; Hannig 2007; Krause 2008; Mederios 2008; Meireles 2010; Bruhn 2012; Costa 2012; Aka 2017).

Secondary outcomes

Eight trials gave patient-reported level of comfort with the treatment (Kugel 2002; Nathoo 2002; Wong 2004; Ziebolz 2007; Ziebolz 2008; Meireles 2010; Auschill 2012; Costa 2012).

Fourteen trials did not report on any adverse reaction after tooth whitening (Nathoo 1994; Cibirka 1999; Russell 1996; Nathoo 2002; Gerlach 2003; Nathoo 2003; Biesbrock 2004; Collins 2004a; Hasturk 2004; Walters 2004; Porciani 2006; Mohan 2008; Meireles 2010; Porciani 2010).

Meireles 2010 in one of his 2-year follow-up reports studied only oral health-related quality of life as an outcome. Two trials have reported oral health-related quality of life along with other outcomes (Wong 2004; Bruhn 2012).

Excluded studies

See Characteristics of excluded studies tables for further details. 22 articles were excluded as they were abstracts of conference presentations (Andreana 2000; Dickinson 2000; Browning 2001; Donly 2001; Godson 2001; Sagel 2001; Smith 2001; Swift 2001; Gerlach 2002d; Lee 2003; Amini 2009; Auschill 2009; Lisante 2009; Anastasia 2010; Archila 2010; Amini 2011; Majeed 2011; Simon 2011; Walter 2011; Garcia-Godoy 2012; Mazur 2013; Perdigao 2013).

We procured 46 full-text articles and excluded them for the following reasons.

- Six trials included studies with in-office bleaching (Burgio 2001; Matis 2005; Zantner 2006; Martin 2015; NCT02603354; NCT02682329).
- Nine trials included children or adolescents in their study (Tam 1999; Donly 2002; Donly 2002a; Loyola-Rodriguez 2003; Gerlach 2004d; Cardoso 2010; Corby 2014; Pinto 2014; Pinto 2017).
- Five trials included studies, which used mechanical method of stain removal like toothbrushing, and whitening dentifrices (Simon 2001; Gerlach 2002c; Gerlach 2003a; Karpinia 2003; Gerlach 2004a).
- One trial reported on home bleaching in which the agent was applied by a professional (Farrell 2006).
- One trial reported the use of a non-whitening chewing gum without an active ingredient (Yankell 1997).
- Of the remaining 24 trials.
  - Nine trials reported only on effects on oral tissues or associated tooth sensitivity or both or were controlled clinical trials (Schulte 1993; Curtis 1996; Jorgensen 2002; Leonard 2002; Collins 2004; Leonard 2007; Farrell 2008; de Geus 2015a; de Geus 2015b).
  - Three trials reported the effects of whitening agents on pulp (Schulte 1994; Fugaro 2004; Fugaro 2005).
  - Four trials reported on the dilution kinetics of whitening agents (Matis 1999; Matis 2002; Gerlach 2004c; Marques 2012).
  - Two studies reported on plaque retention post-bleaching (Schiff 1994; Gursoy 2008).
  - One study reported on oral microflora (Alkmin 2005).
  - One study reported on the effect of a desensitising agent (Leonard 2004).
  - One study reported on the effect of coffee exposure on bleaching (Rezende 2013).
  - One study reported the effect of bleaching on orthodontic brackets (Jadad 2011).
  - One study reported the effect of two different tray designs used during bleaching (Matis 2002a).
  - One study reported the efficacy of using a chromameter to assess bleaching (Gerlach 2002e).

Studies awaiting classification

See Characteristics of Characteristics of studies awaiting classification tables for further details.

- Twelve studies had incomplete or missing data; hence, we could not use them for analysis (Gegauff 1993; Reinhardt 1993; Rosenstiel 1996; Barnes 1998; Pohjola 2002; Ozcan 2003; Browning 2004; Ferrari 2004; Gambarini 2004; Braun 2007; Shin 2010; Simon 2014).
- We are awaiting full texts for eight published trials (Heymann 1998; Sielski 2003; Gerlach 2004b; Guerrero 2007; Bizhang 2017; Kim 2018; Maran 2018; Rossi 2018).
- Two studies were protocol registration of completed studies, but we could not access the full text (NCT02151058; NCT03217994).

Ongoing studies

- One clinical trial has not yet published the results and is ongoing (NCT03026725).

Risk of bias in included studies

See Figure 2 for details.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

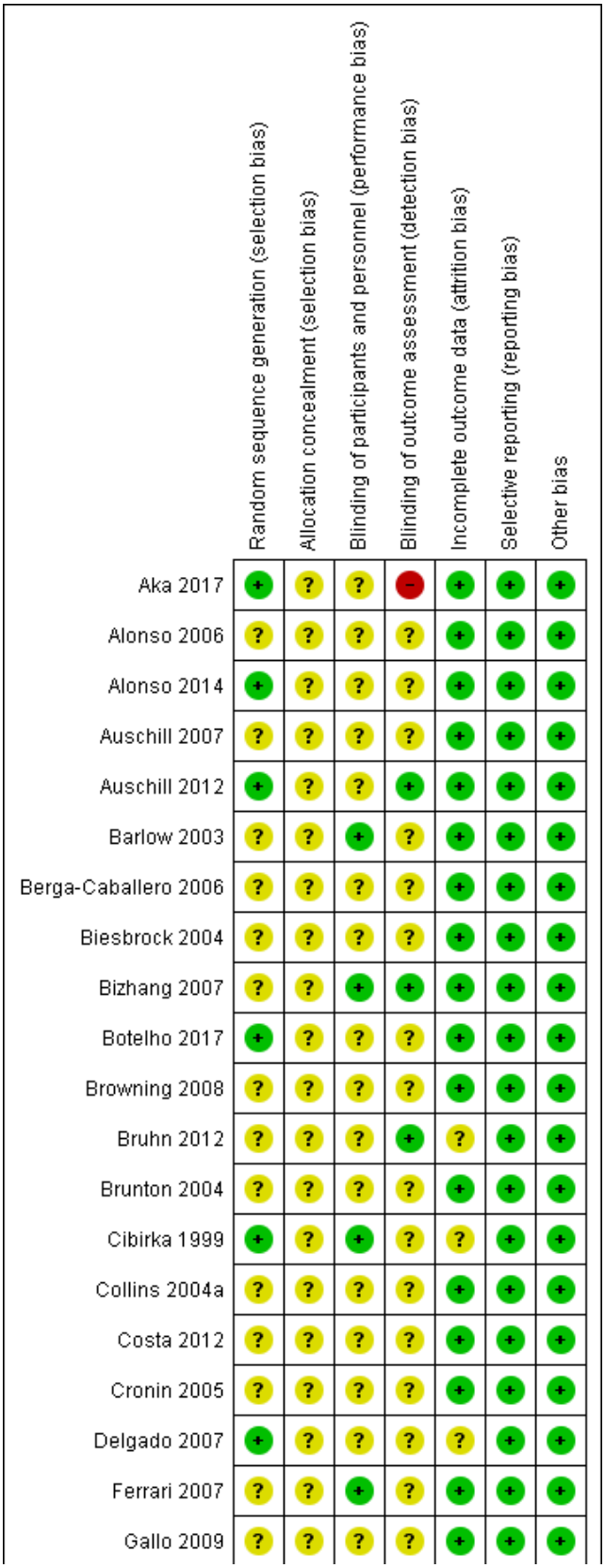


Figure 2. (Continued)

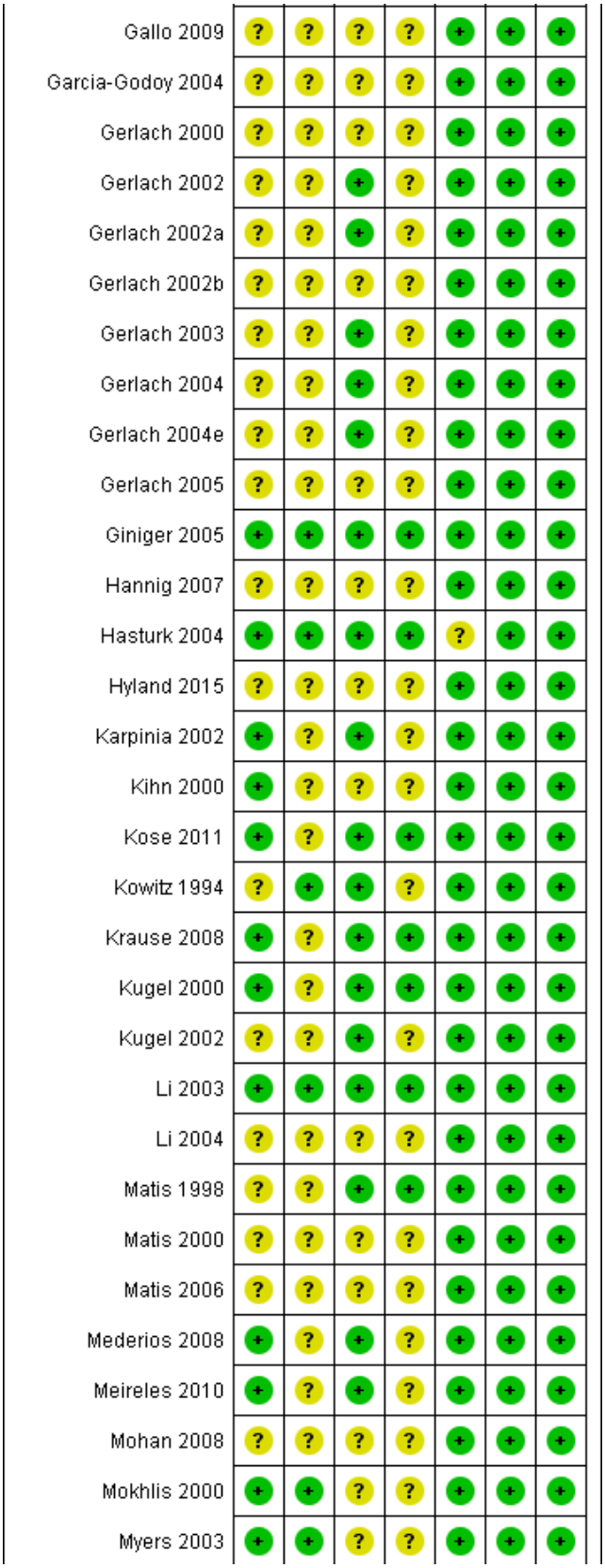
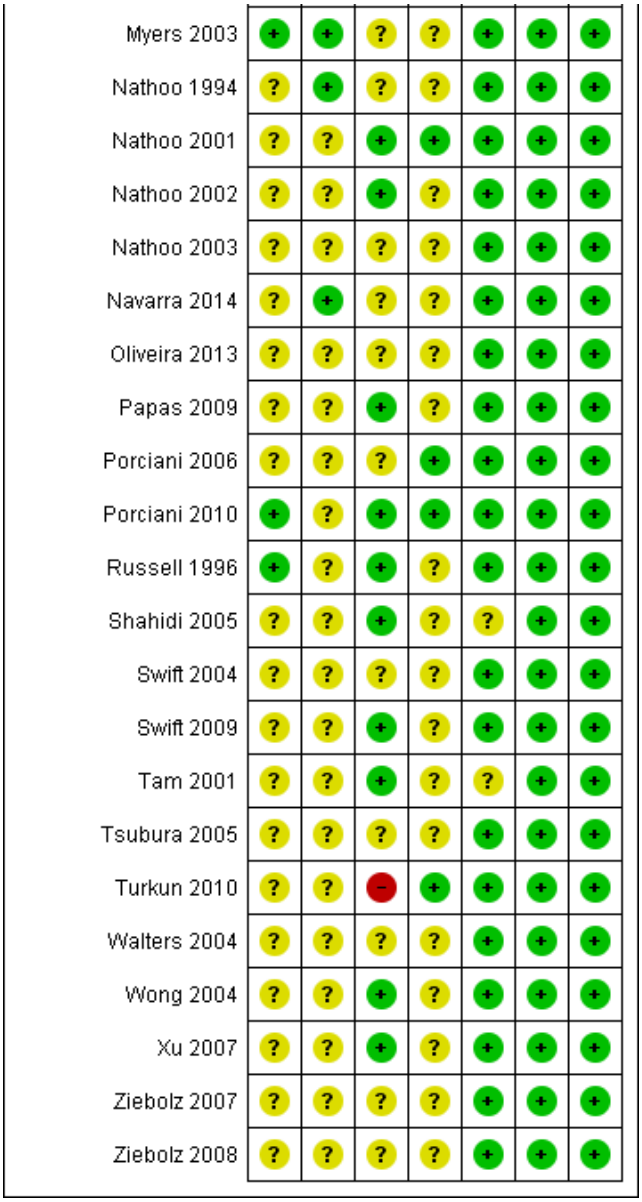


Figure 2. (Continued)



Allocation

Twenty of the included trials reported the method of sequence generation and were at a low risk of bias (Russell 1996; Cibirka 1999; Kihn 2000; Mokhlis 2000; Karpinia 2002; Kugel 2002; Li 2003; Myers 2003; Hasturk 2004; Giniger 2005; Delgado 2007; Krause 2008; Mederios 2008; Meireles 2010; Porciani 2010; Kose 2011; Auschill 2012; Alonso 2014; Aka 2017; Botelho 2017); the remaining trials were at an unclear risk of bias.

Eight of the included studies reported concealment of allocation (Kowitz 1994; Nathoo 1994; Mokhlis 2000; Li 2003; Myers 2003; Hasturk 2004; Giniger 2005; Navarra 2014). The rest of the trials were marked unclear.

Blinding

Out of 71 included trials, blinding of participants and personnel was unclear in 39 trials (Nathoo 1994; Gerlach 2000; Kihn 2000; Matis 2000; Mokhlis 2000; Gerlach 2002b; Myers 2003; Nathoo 2003; Biesbrock 2004; Brunton 2004; Collins 2004a; Garcia-Godoy 2004; Li 2004; Swift 2004; Walters 2004; Cronin 2005; Gerlach 2005; Tsubura 2005; Alonso 2006; Berga-Caballero 2006; Matis 2006; Porciani 2006; Auschill 2007; Delgado 2007; Hannig 2007; Ziebolz 2007; Browning 2008; Mohan 2008; Ziebolz 2008; Gallo 2009; Auschill 2012; Bruhn 2012; Costa 2012; Oliveira 2013; Alonso 2014; Navarra 2014; Hyland 2015; Aka 2017; Botelho 2017) and high in one (Turkun 2010); 31 trials had reported satisfactory blinding of participants and personnel.

Blinding of assessors was reported in 14 trials and were at a low risk of detection bias (Matis 1998; Kugel 2000; Nathoo 2001; Kugel 2002; Li 2003; Hasturk 2004; Giniger 2005; Porciani 2006; Bizhang 2007; Krause 2008; Porciani 2010; Turkun 2010; Auschill 2012; Bruhn 2012).

Aka 2017 was at a high risk of detection bias due to lack of clarity of how teeth were selected for outcome assessment.

The other 56 were marked unclear as the trials described their studies as 'double-blinded', but no details of assessor blinding were given, or were single-blinded studies (Kowitz 1994; Nathoo 1994; Russell 1996; Cibirka 1999; Gerlach 2000; Kihn 2000; Matis 2000; Mokhlis 2000; Tam 2001; Gerlach 2002; Gerlach 2002a; Gerlach 2002b; Karpinia 2002; Nathoo 2002; Barlow 2003; Gerlach 2003; Myers 2003; Nathoo 2003; Biesbrock 2004; Brunton 2004; Collins 2004a; Garcia-Godoy 2004; Gerlach 2004; Gerlach 2004e; Li 2004; Swift 2004; Walters 2004; Wong 2004; Cronin 2005; Gerlach 2005; Shahidi 2005; Tsubura 2005; Alonso 2006; Berga-Caballero 2006; Matis 2006; Auschill 2007; Delgado 2007; Hannig 2007; Ferrari 2007; Xu 2007; Ziebolz 2007; Browning 2008; Mederios 2008; Mohan 2008; Ziebolz 2008; Gallo 2009; Papas 2009; Swift 2009; Meireles 2010; Kose 2011; Costa 2012; Oliveira 2013; Alonso 2014; Navarra 2014; Hyland 2015; Botelho 2017).

Incomplete outcome data

Six trials (Cibirka 1999; Tam 2001; Hasturk 2004; Shahidi 2005; Delgado 2007; Bruhn 2012) were marked unclear for risk of attrition bias as the trials did not mention any details about dropouts and there was a mismatch between the number randomised and number analysed.

Selective reporting

All 71 trials were at a low risk of bias for selective reporting.

Other potential sources of bias

All 71 trials were at a low risk for other bias.

Overall risk of bias

Two studies were at low overall risk of bias (Li 2003; Giniger 2005); two at high overall risk of bias (Turkun 2010; Aka 2017); and the remaining 67 at unclear overall risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** CP gel in tray versus placebo for whitening teeth; **Summary of findings 2** HP gel in tray versus placebo for whitening teeth; **Summary of findings 3** HP strips versus placebo for whitening teeth; **Summary of findings 4** CP paint-on gel versus placebo for whitening teeth; **Summary of findings 5** HP paint-on gel versus placebo for whitening teeth; **Summary of findings 6** SHMP chewing gum versus placebo for whitening teeth; **Summary of findings 7** STPP chewing gum versus placebo for whitening teeth; **Summary of findings 8** HP mouthwash versus placebo for whitening teeth; **Summary of findings 9** CP gel in tray versus CP gel in tray for whitening teeth; **Summary of findings 10** CP gel in tray versus HP gel in tray for whitening teeth; **Summary of findings 11** HP strips versus CP gel in tray for whitening teeth; **Summary of findings 12** HP strips versus HP gel in tray for whitening teeth; **Summary of findings 13** HP strips versus HP strips (different concentrations) for whitening teeth; **Summary of findings 14** CP paint-on gel versus HP strips for whitening teeth; **Summary of findings 15** HP paint-on gel versus HP strips for whitening teeth; **Summary of findings 16** CP paint-on versus CP paint-on (different concentrations) for whitening teeth; **Summary of findings 17** CP paint-on versus HP paint-on for whitening teeth; **Summary of findings 18** HP paint-on versus HP paint-on for whitening teeth; **Summary of findings 19** SPC paint-on versus CP paint-on for whitening teeth

In our review, we tried to do the analyses based on duration as early effects, intermediate effects and long-term effects. However due to high heterogeneity, many trials could not be combined in the individual categories. Also not many trials reported long-term effects of bleaching agents. We also felt that combining varying methods of application and concentrations would not give a clearer picture to the customers who would want to choose among the different products available over-the-counter. With these considerations in mind, we chose to conduct the analyses based on the concentration of active agents and method of application. Only those trials having all the variables (concentration, active agent, method and timing of application and duration) similar were combined in meta-analyses. The rest of the comparisons were reported independently.

As most of the trials reported data at multiple time points, the longest follow-up time was considered in the meta-analysis as described by the *Cochrane Handbook for Systematic Reviews of Interventions* section 9.3.4 (Higgins 2011). However, the other time points have also been discussed descriptively wherever relevant, as bleaching effect at the shorter time duration may have clinical implications. We discussed all the outcomes separately in the individual comparisons for ease of understanding.

1. Bleaching agent versus placebo

1a. CP gel in tray versus placebo

Tooth whitening - assessed by the dentist

Six trials studied carbamide peroxide (CP) versus placebo (Russell 1996; Matis 1998; Browning 2008; Mederios 2008; Hyland 2015; Aka 2017) with Russell 1996 and Matis 1998 expressing dichotomous data. Browning 2008; Hyland 2015; and Aka 2017 were the multiarm trials from which we analysed data comparing CP gel in tray to placebo. Mederios 2008 was described qualitatively and not included in meta-analyses as the data were represented as median scores.

Continuous outcome

Hyland 2015 and Aka 2017 used the digital images with CIEL*a*b* scoring while Browning 2008 and Mederios 2008 used the Vita shade guide. Aka 2017 analysed the groups based on baseline tooth shade as light shade, medium dark and dark shades. In all categories, the test group showed favourable results for whitening of teeth compared to placebo gel.

Hyland 2015 compared 5% CP formulation containing sodium tripolyphosphate for 2 weeks and showed L* values significantly higher compared to placebo group (mean difference (MD) 4.56, 95% confidence interval (CI) 1.52 to 7.59; 1 trial, 21 participants; Analysis 1.1).

Browning 2008 used 10% CP with a desensitiser versus placebo gel for 2 weeks with the test group showing better Vita shade scores for lightness compared to placebo (MD 4.70, 95% CI 3.28 to 6.12; 1 trial, 37 participants; Analysis 1.1).

Irrespective of the original shade, the CP group showed significantly higher E values compared to placebo in Aka 2017 (light shade: MD 4.50, 95% CI 4.04 to 4.96; 1 trial, 179 teeth; medium dark

shade: MD 6.90, 95% CI 6.35 to 7.45; 1 trial, 172 teeth; darker shade: MD 10, 95% CI 9.44 to 10.56; 1 trial, 176 teeth) (Analysis 1.1).

Mederios 2008 compared 10% CP to placebo for 21 days and presented data as a medium score and interquartile range. The median increase in lightness of the teeth in the test group was 3 units based on the value-ordered Vitapan shade guide. This improvement in lightness was maintained for 6 months in 88% of this group. In the placebo group, 8% has a 2-unit reduction in tooth colour at day 21.

Dichotomous outcome

Russell 1996 and Matis 1998 studied the effect of 10% CP and the data at 2 weeks and 6 months for these trials were combined in the meta-analysis. Russell 1996 used the Vita shade guide an categorised the scale for measurement as darker, same or lighter. The lighter shade score was considered as events. Matis 1998 used an ordinal scale where 0 represented no change; 1 represented slight change; 2 was moderate change and 3 represented a large colour change. Scores 2 and 3 were combined and considered as events.

A significant lightening effect was shown at 2 weeks. In addition, the lightening effect lasted when tested at 6 months for the majority of the subjects (risk ratio (RR) 6.74, 95% CI 3.15 to 14.40; 2 trials, 109 participants; Analysis 2.1). Russell 1996 showed similar results at 1 week, 6 weeks and 3 months interval. Matis 1998 also showed similar results at 4 weeks.

Tooth whitening - reported by the patient

Mederios 2008 recorded volunteers satisfaction by administering a questionnaire at the end of 21 days of treatment and Aka 2017 reported patient satisfaction after 10 days, 14 days, 2 weeks and 6 months of bleaching, which was self-assessed on a 7-point scale, with 1 correlating to no satisfaction and 7 to maximum satisfaction. Patients in the CP group were more satisfied by the bleaching effect in both the trials.

Adverse effects

Most common adverse effects were gingival sensitivity, tooth sensitivity, gastrointestinal sensitivity in both the groups although they were transient and mild (Matis 1998). Sensitivity to hot and cold, gingival sensitivity, tongue and throat sensitivity was reported by Myers 2003 which was more for the test group. Mederios 2008 also reported tooth sensitivity, which was more for the CP group compared to the placebo group.

Other trials did not report any adverse reactions. No other secondary outcomes were reported.

1b. HP gel in tray versus placebo

Tooth whitening - assessed by the dentist

Two trials studied the effect of hydrogen peroxide (HP) gel versus placebo (Myers 2003; Mohan 2008). Mohan 2008 reported significantly greater L* values at 3, 7 and 14 days in the 6% HP gel group indicating greater lightness (14 days: MD 3.08, 95% CI 2.28 to 3.88; 1 trial, 49 participants; Analysis 3.1).

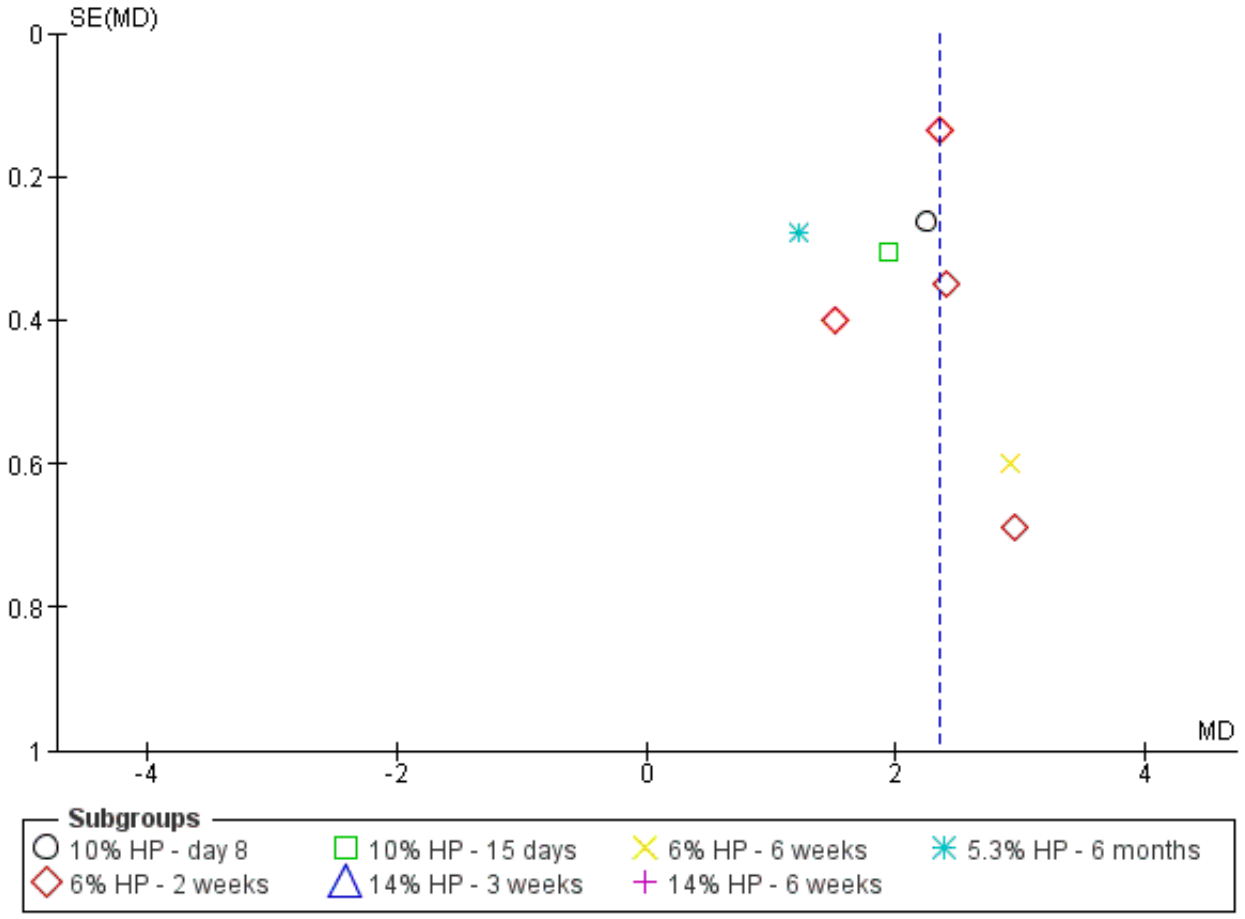
Myers 2003 used Vita shade guide and found the 3% HP group with significantly lighter shades at 2, 12 and 26 weeks compared to the placebo group. Mean shade change was 4.2 Vita shade tabs at 2 weeks. At 26 weeks (6 months), the degree of whitening was 4.1 tabs.

No other outcomes were reported.

1c. HP strips versus placebo

See Figure 3.

Figure 3. Funnel plot of comparison: 4 HP strip versus placebo, outcome: 4.1 Tooth whitening - assessed by the dentist.



Tooth whitening - assessed by the dentist

Ten trials studied the effect of HP strips against placebo (Kugel 2000; Gerlach 2002; Garcia-Godoy 2004; Gerlach 2004e; Swift 2004; Wong 2004; Bizhang 2007; Papas 2009; Swift 2009; Bruhn 2012).

Gerlach 2004e who studied 10% HP for 8 days against a placebo showed greater L* value for the test group indicating better lightness (MD 2.24, 95% CI 1.72 to 2.76; 1 trial, 36 participants; Analysis 4.1).

The Kugel 2000; Wong 2004; Bizhang 2007; Swift 2009 trials were combined to analyse the effect of 6% / 5.3% HP versus placebo for 2 weeks. L* values significantly higher in the HP group indicated greater lightness compared to placebo (MD 2.24, 95% CI 1.83 to 2.66; 4 trials, 195 participants; Analysis 4.1).

Papas 2009 showed similar results as Gerlach 2004e at 15 days (MD 1.93, 95% CI 1.34 to 2.52; 1 trial, 40 participants; Analysis 4.1).

Swift 2004 and Garcia-Godoy 2004 studied 14% HP versus placebo for 3 weeks and 6 weeks, using Vita shade guide and CIEL*a*b* scoring respectively. The 14% HP group demonstrated improvement in shades relative to the placebo strip group with a difference between treatment groups favouring the peroxide group in both trials (Swift 2004: MD 7.60, 95% CI 6.18 to 9.02; 1 trial, 28 participants; Garcia-Godoy 2004: MD 5.16, 95% CI 4.21 to 6.11; 1 trial, 35 participants (Analysis 4.1)).

Swift 2009 reported the HP group with better lightening effect compared to placebo at 4 weeks and 6 weeks (6 weeks: MD 2.90, 95% CI 1.73 to 4.07; 1 trial, 37 participants; Analysis 4.1).

5.3% HP versus placebo studied by Gerlach 2002e showed that most of the initial colour change remained at 6 months post-treatment with the whitening strip group continuing to demonstrate highly significant improvements in tooth colour relative to the placebo group (MD 1.21, 95% CI 0.67 to 1.75; 1 trial, 52 participants; Analysis 4.1).

Tooth whitening - reported by the patient

One trial (Bruhn 2012) compared 14% HP against placebo and reported the tooth colour satisfaction scale (TCSS). One trial (Wong 2004) reported patient satisfaction, rated using a product satisfaction questionnaire. Satisfaction regarding the whitening effect of the product was highest for the strip group compared to the placebo group in both trials.

Adverse effects

Treatment with HP whitening strips was generally well tolerated with adverse events confined to symptoms only. Mild and transient

tooth sensitivity and oral irritation were the most common adverse events reported in most of the trials (Kugel 2000; Gerlach 2002e; Garcia-Godoy 2004; Gerlach 2004e; Swift 2004; Papas 2009; Swift 2009).

Oral health-related quality of life

One trial (Bruhn 2012) compared 14% HP strips against placebo and reported the oral health-related quality of life (OHRQoL). Wong 2004 reported the standardised response mean for the oral health impact profile (OHIP) and its domains for subjects in each category of the global transition judgement on whether they were dissatisfied (-1), neutral (0) or satisfied (1). No significant impact of tooth whitening was found in both trials on OHRQoL.

No trial reported on patient's level of comfort with treatment.

1d. CP paint-on gel versus placebo

Tooth whitening - assessed by the dentist

Nathoo 2002 compared 18% CP gel to placebo using Vita shade guide and the mean changes from baseline tooth shade rank score were compared across treatment groups. CP paint-on gel exhibited a mean change score of 2.54 units greater that placebo at 2 weeks interval and 3.5 units higher at 3 weeks interval (3 weeks: MD 3.50, 95% CI 3.12 to 3.88; 1 trial, 77 participants; Analysis 5.1).

Patient comfort

In Nathoo 2002 participants anecdotally reported that the products were extremely easy to apply and did not interfere with speech or life style.

No other outcomes were reported.

1e. HP paint-on gel versus placebo

Tooth whitening - assessed by the dentist

Collins 2004a used Vita shade and Xu 2007 used digital image analysis with CIEL*a*b* scoring to test 6% HP paint-on gel versus placebo**.** We combined the 2-week data using standardised mean difference (SMD) and the paint-on group exhibited greater whitening compared to placebo (SMD 0.67, 95% CI 0.19 to 1.14; 2 trials, 148 participants; Analysis 6.1). Similar results were found by Collins 2004a at 1 week interval.

Adverse effects

Collins 2004a reported the HP group participants with more gum irritation (reddening) compared to placebo although the symptoms were mild. One case of tooth sensitivity was noted.

No other outcomes were reported.

1f. SHMP chewing gum versus placebo

Tooth whitening - assessed by the dentist

Among the three trials comparing sodium hexametaphosphate (SHMP) chewing gum to placebo, Biesbrock 2004 used digital image analysis with CIEL*a*b* scoring using 7.5% SHMP; Walters 2004 and Porciani 2006 used the Lobene stain index with 5.65% and 4% SHMP respectively. Accumulation of stain in all the trials was lower in the test group compared to placebo in Biesbrock 2004 at 1 day and 2 days (2 days: MD 0.89, 95% CI 0.77 to 1.01; 1 trial, 37 participants; Analysis 7.1); Walters 2004 at 3 days (MD 2.60, 95% CI 1.45 to 3.75; 1 trial, 20 participants; Analysis 7.1) also found the test group exhibiting lesser stains compared to placebo.

Porciani 2006 reported 33% reduction in induced stain formation by the test group compared to placebo at 12 weeks (MD -0.14, 95% CI -0.38 to 0.10; 1 trial, 108 participants; Analysis 7.1).

No other outcomes were reported.

1g. STPP chewing gum versus placebo

Tooth whitening - assessed by the dentist

Porciani 2010 studied 1% sodium tripolyphosphate (STPP) against a placebo using Lobene composite stain index which was reduced by 8.8% in the test group and increased by 8% in the control group (MD 0.18, 95% CI 0.10 to 0.26; 1 trial, 108 participants; Analysis 8.1).

No other outcomes were reported.

1h. HP mouthwash versus placebo

Tooth whitening - assessed by the dentist

Hasturk 2004 evaluated the tooth whitening effect of 1.5% HP fluoridated rinse by dichotomising the change in shades as measured by the Lobene stain index. Data were expressed in odds ratios (OR) at 1 month, 3 months, 6 months and overall tooth whitening. Generic inverse variance method was used and log of odds ratio and standard error were calculated for the analysis.

Compared with placebo, the HP mouthrinse group was more than 7 times as likely to show whitening at 1 month and 3 months. Greater whitening was also demonstrated by the mouthwash group at 6 months (OR 10.89, 95% CI 5.08 to 23.35; 1 trial, 78 participants; Analysis 9.1). Overall tooth whitening was almost 8.7 times more likely among the mouthwash group than the placebo group.

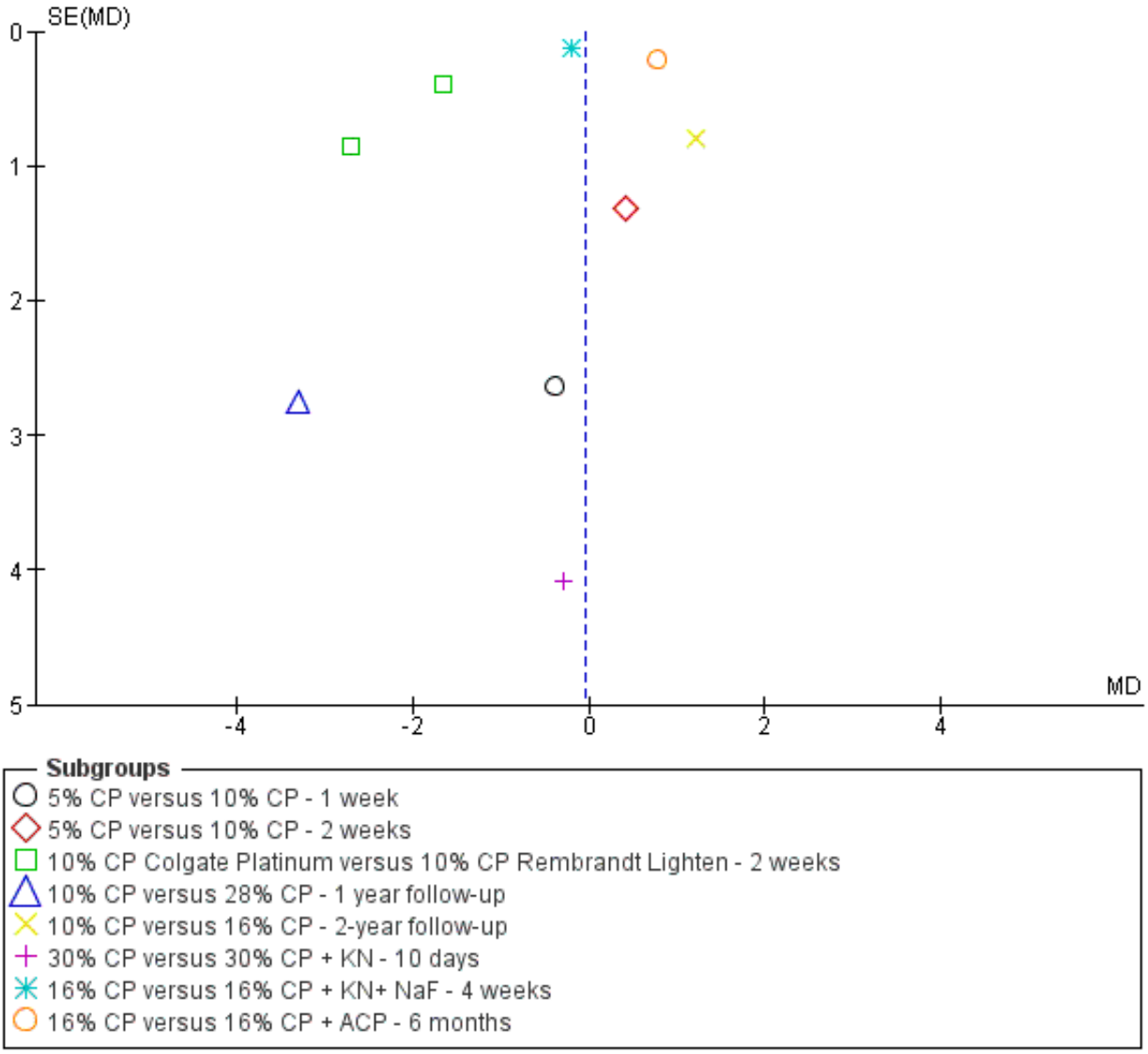
No other outcomes were reported.

2. Bleaching agent versus bleaching agent

2a. CP tray versus CP tray

See Figure 4.

Figure 4. Funnel plot of comparison: 11 CP tray versus CP tray, outcome: 11.1 Tooth whitening - assessed by the dentist.



Among the 18 trials, six used value-oriented/Vita classical shade guide for measuring colour change (Cibirka 1999; Kihn 2000; Giniger 2005; Browning 2008; Gallo 2009; Kose 2011).

Seven trials used electronic instruments for colour change analysis (spectrophotometer, colorimeter, digital analysis) with CIEL*a*b* scoring system (Kowitz 1994; Matis 2000; Tsubura 2005; Matis 2006; Turkun 2010; Navarra 2014; Hyland 2015).

Three trials (Mokhlis 2000; Nathoo 2001; Meireles 2010) measured whitening using a combination of shade guide and electronic instruments. All these trials reported data in CIEL*a*b* scoring which was considered for analysis.

Krause 2008 reported patient contentment using inter-personal modal intensity comparison where the patient pressed the bulb of a manometer in proportion to their objective concerning the bleaching outcome.

Meireles 2010 in one of his follow-up reports used oral impact on daily performance (OHIP) scoring to assess oral health-related quality of life.

Tam 2001 used photographic evaluation and visual analogue scale (VAS), which the patients marked daily in the evening before the next day's bleaching treatment.

Tooth whitening - assessed by the dentist

Dichotomous outcome

Data were presented as an ordinal scale of darker, same or lighter in Cibirka 1999 trial. Number of participants in the lighter shade category were considered as events. A significant degree of lightening of tooth shade relative to baseline values at 2 weeks was demonstrated for both Opalescence and NiteWhite Excel (10% CP formulations), however no evidence of a difference was found

between the groups (RR 1.03, 95% CI 0.90 to 1.18; 1 trial, 66 participants; Analysis 10.1).

Continuous outcome

Nathoo 2001 which compared 5% and 10% CP found no evidence of a difference between the groups. Mean unit change after 7 days for 5% group was 6.7±1.9 while for the 10% group was 5.7±2 though the result was not statistically significant (MD -0.38, 95% CI -5.55 to 4.79; 1 trial, 58 participants; Analysis 11.1).

Hyland 2015 a multiarm trial compared 5% and 10% CP with STPP formulations. It found no evidence of a difference between 55% and 10% CP in tooth whitening at 2 weeks following daily wear of tooth whitening trays for 2 hours a day (MD 0.41, 95% CI -2.17 to 2.98; 1 trial, 21 participants; Analysis 11.1).

Colgate Platinum (CLP) and Rembrandt Lighten (RL) (both 10% CP formulations) compared in Kowitz 1994; Nathoo 1994, showed significantly higher L* values for the CLP group compared to the RL group (MD -1.92, 95% CI -2.80 to -1.03; 2 trials, 88 participants; Analysis 11.1).

Both daytime at-home bleaching system including 28% CP gel with a non-custom tray (Meta tray) and conventional overnight at-home 10% CP gel with a custom tray (Opalescence PF) in Turkun 2010 produced whitening compared to the baseline. Intergroup comparison showed 10% CP overnight bleaching group to be superior to the day time 20-minute bleaching at 2 weeks and 1 year follow-up (1 year follow-up: MD -3.30, 95% CI -8.71 to 2.11; 1 trial, 20 participants; Analysis 11.1).

Follow-up at 2 years (Meireles 2010) (MD 1.20, 95% CI -0.35 to 2.75; 1 trial, 81 participants; Analysis 11.1) revealed that the tooth shade remained significantly lighter compared to baseline in both the groups comparing 10% and 16% CP. However, tooth shade relapse showed no difference between the groups.

Gallo 2009 who used different concentrations of CP with and without desensitisers, showed no significant difference between the groups in terms of colour change at 10 days (MD -0.30, 95% CI -8.28 to 7.68; 1 trial, 40 participants; Analysis 11.1). Similar results were observed in Kose 2011 at 4 weeks (MD -0.20, 95% CI -0.44 to 0.04; 1 trial, 60 participants; Analysis 11.1).

At 180 days the amorphous calcium phosphate (ACP) group retained nearly 10% more of their original whitening treatment result compared to control in Giniger 2005 (MD 0.78, 95% CI 0.37 to 1.19; 1 trial, 27 participants; Analysis 11.1).

Polanight (PN) and Opalescence (OP) (both 10% CP formulations) compared in Tsubura 2005, showed significant difference in L* values for PN compared to OP. Bleaching with PN was considered more effective than that with OP in young patient group and in women (MD 1.46, 95% CI 0.13 to 2.79; 1 trial, 116 participants; Analysis 11.2).

Five-year data of 10% CP versus 15% CP was analysed from Matis 2006. No evidence of a difference was found between the groups in relation to shade change (MD -1.47, 95% CI -3.56 to 0.62; 1 trial, 58 participants; Analysis 11.2).

Kihn 2000 showed the 15% CP group to have a larger amount of shade change than did the control group (MD 1.65, 95% CI 0.22 to 3.08; 1 trial, 52 participants; Analysis 12.1). Matis 2000 also showed similar results (MD 2.22, 95% CI 1.29 to 3.15; 1 trial, 25 participants; Analysis 12.2).

Data for 10% CP with and without potassium nitrate and sodium fluoride used in two trials (Browning 2008; Navarra 2014), was combined in the meta-analysis and showed no evidence of a difference between the whitening systems (standardised mean difference (SMD) 0.32, 95% CI -0.20 to 0.84; 2 trials, 58 participants; Analysis 12.3).

Tooth whitening - reported by the patient

Krause 2008 reported patient contentment with the bleaching outcome with an inter-modal intensity comparison. Although the patient contentment score in the 17% group was higher, no evidence of a difference was found between both groups at 2 weeks and 3 weeks interval (3 weeks: MD 2.60, 95% CI 2.57 to 2.63; 1 trial, 20 participants; Analysis 11.3). All participants completing the 2-year evaluation in Meireles 2010 reported no evidence of a difference between treatment groups regarding the patient-reported satisfaction in relation to whitening and retention of whitening. Meireles used a questionnaire to rate patient satisfaction regarding whitening outcome in one of his follow-up reports. No evidence of a difference in the whitening effect was found as reported by patients in both CP 10% and CP 16% groups.

In Matis 2006, at the 5th year evaluation appointment, seven were very pleased with how their teeth look at that time in both 10% and 15% groups. 14 of them were very pleased and seven reported they were not pleased with the appearance in both groups.

Tam 2001 presented data in range using the VAS scale reported by the patients. We did not use these values for analysis according to the *Cochrane Handbook for Systematic Reviews of Interventions* section 7.7.3.6 (Higgins 2011). The authors reported the lack of evidence of a difference in perceived whiteness between the groups with and without the desensitiser.

Patient comfort

One of Meireles 2010 follow-up reports used a questionnaire to rate patient comfort on 1 to 5 scale (1 representing agree and 5 representing disagree). Participants from both whitening regimens reported positive opinions about the treatment. Despite this, the CP 10% group reported less interference with the tray when talking (P = 0.02) and less discomfort after application (P = 0.04) compared to the CP 16% group.

Adverse effects

Higher concentrations of CP had more sensitivity compared to lower concentrations (Nathoo 2001; Matis 2006; Krause 2008; Meireles 2010). Navarra 2014 and Browning 2008 reported bleaching agents with desensitiser with significantly lower sensitivity than the bleaching product that did not contain desensitising agents. Kihn 2000; Matis 2000; Gallo 2009 did not report any significant difference in the tooth and gingival irritation between the two groups. Tam 2001; Giniger 2005; Tsubura 2005; Kose 2011 reported mild irritation and sensitivity in both groups. Kowitz 1994; Nathoo 1994; Cibirka 1999; Turkun 2010; Hyland 2015 did not report any adverse events.

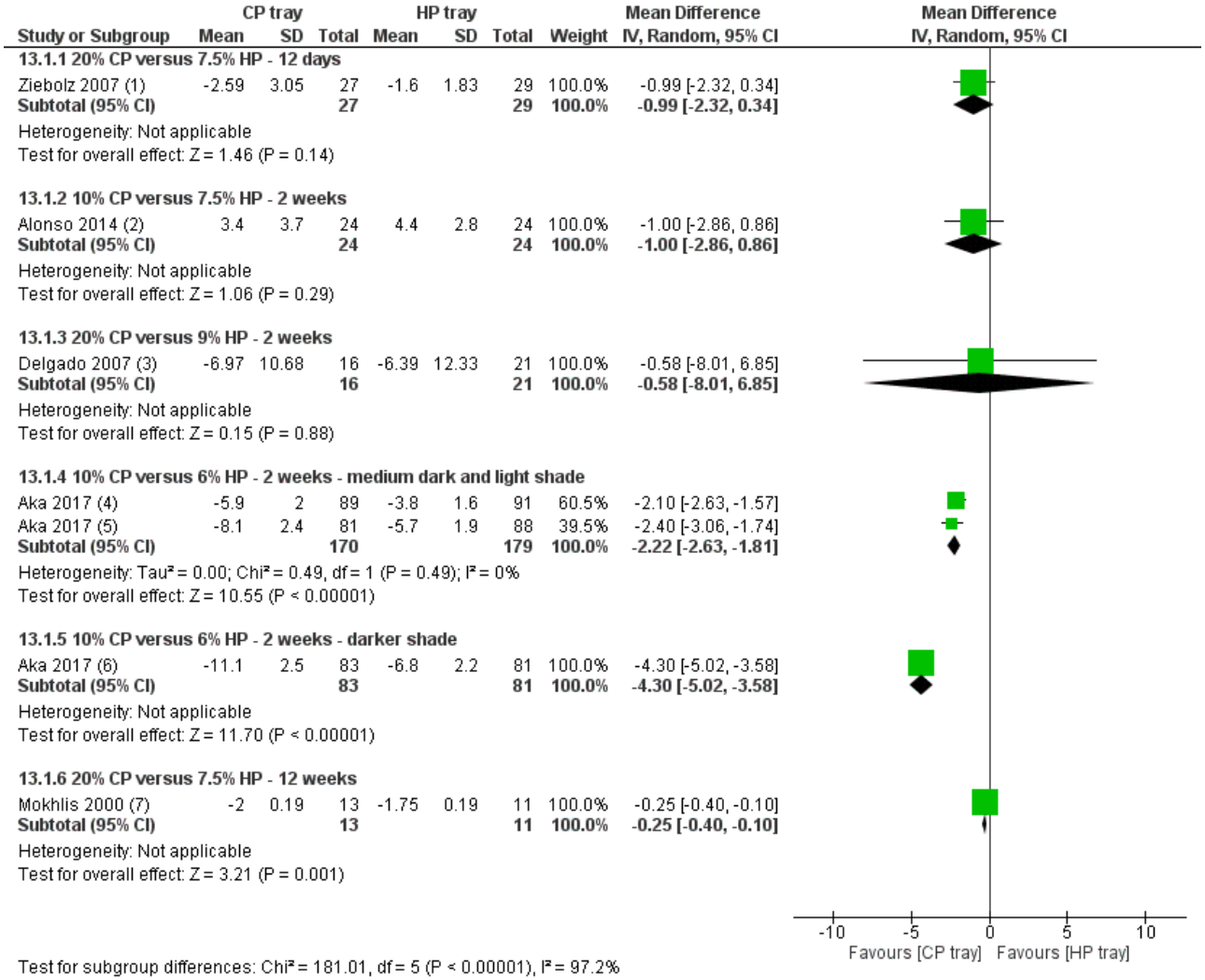
Oral health-related quality of life

In Meireles 2010 2-year follow-up report the 16% CP group showed greater bleaching effect than 10% CP, however, OHRQoL was similar for both groups.

2b. CP tray versus HP tray

See Figure 5.

Figure 5. Forest plot of comparison: 13 CP tray versus HP tray, outcome: 13.1 Tooth whitening - assessed by the dentist.



Footnotes

(1) Group 1: 20% CP; Group 2: 7.5% HP. CIELAB scoring was used. Greater value indicates better lightness.
(2) Group 1: 7.5 % HP; Group 2: 10% CP. Vita shade guide was used.Greater value indicates better lightness.
(3) Group 1: 20% CP; Group 2: 9% HP. Vita shade guide was used.Greater value indicates better lightness.
(4) (Tooth level analysis) Group 1: 10% CP; Group 2: 6% HP for lighter teeth. CIELAB scoring used.Greater value indicates better lightness.
(5) (Tooth level analysis) Group 1: 10% CP; Group 2: 6% HP for medium dark teeth after 14 days of bleaching. CIELAB scoring was used.
(6) (Tooth level analysis) Group 1: 10% CP; Group 2: 6% HP for darker teeth after 14 days of bleaching. CIELAB scoring was used.
(7) Group 1: 20% CP; Group 2: 7.5% HP. CIELAB scoring was used.Greater value indicates better lightness.

Tooth whitening - assessed by the dentist

Among the seven trials, three used value-oriented/Vita classical shade guide for measuring colour change (Alonso 2006; Berga-Caballero 2006; Delgado 2007). Two trials used electronic instruments for colour change analysis (spectrophotometer, colorimeter, digital analysis) with CIEL*a*b* scoring system (Ziebolz 2007; Alonso 2014). Two trials (Mokhlis 2000; Aka 2017) measured whitening using a combination of shade guide and electronic instruments. All these trials reported data in CIEL*a*b* scoring which was considered for analysis.

Both 7.5% HP and 20% CP in Ziebolz 2007 resulted in significant colour improvements in all parameters compared to baseline. Though the reduction in yellowness was significantly more in the 20% CP group compared to 7.5% HP, improvement in lightness (L*)

showed no evidence of a difference over the 12 days period (MD -0.99, 95% CI -2.32 to 0.34; 1 trial, 56 participants; Analysis 13.1).

We compared 10% CP to 7.5% HP used in a multiarm trial (Alonso 2014). There was no evidence of a difference between the groups though there was an increase in lightness compared to baseline in both groups (MD -1, 95% CI -2.86 to 0.86; 1 trial, 48 participants; Analysis 13.1).

Delgado 2007 9% HP group showed a statistically significant 1.54 greater shade rank score unit reduction in the mean tooth shade rank score after 5 days. However, after 7 and 14 days the rank greater score unit reductions were 1.18 and 0.83 for the 9% HP group compared to the 20% CP group, but not statistically significant (MD -0.58, 95% CI -8.01 to 6.85; 1 trial, 37 participants; Analysis 13.1).

Irrespective of the original shade, 10% CP bleaching groups in Aka 2017 multiarm trial showed significantly higher E values compared to 6% HP: medium dark and light shade: MD -2.22, 95% CI -2.63 to -1.81; 2 trials, 349 teeth; darker shade: MD -4.30, 95% CI -5.02 to -3.58; 1 trial, 164 teeth (Analysis 13.1).

Similar concentrations of CP and HP were used in another trial (Mokhlis 2000) which favoured the 20% CP group for better lightness in the first 14 days. But at the end of the study there was no evidence of a difference between the two groups (12 weeks: MD 0.25, 95% CI 0.10 to 0.40; 1 trial, 24 participants; Analysis 13.2).

Berga-Caballero 2006 found that the changes in colour ranged from 1 to 10 shades of the Vita shade guide's brightness-based classification; the whitening success percentage was between 315% and 100% on the Jane-Roig scale, which is based on the greatest percentage of whitening that can be achieved in a tooth, depending on its initial colour. Both 10% CP applied for varying times and 3.5% HP were effective.

Alonso 2006 reported no evidence of a difference between the groups using 3.5% HP along with a desensitiser (potassium nitrate) versus 10% CP.

Tooth whitening - reported by the patient

Aka 2017 reported that the 10% CP/PF (Opalescence PF) groups were more satisfied with the bleaching effect than those in the 6% HP groups.

Patient comfort

In Ziebolz 2007 both 7.5% HP and 10% CP groups showed a similar proportion of subjects with complaints regarding comfort of the bleaching treatment with no significant differences on a 4-point ordinal scale.

Adverse effects

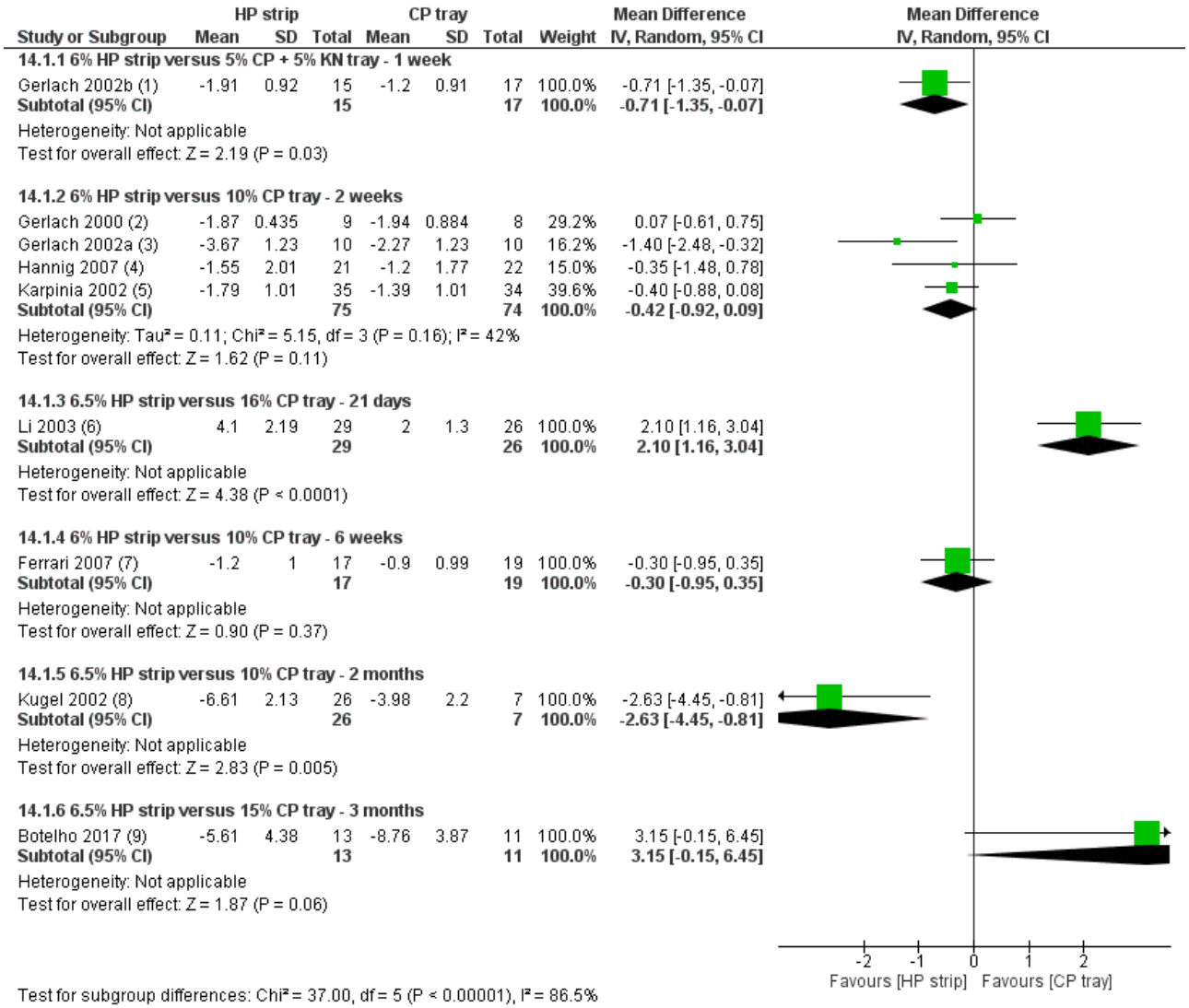
Mokhlis 2000; Ziebolz 2007; Aka 2017 did not report any significant difference in the tooth and gingival irritation between the two groups. Alonso 2006; Berga-Caballero 2006; Delgado 2007; Alonso 2014 reported mild irritation and sensitivity in both groups.

No other outcomes were reported.

2c. HP strips versus CP tray

See Figure 6.

Figure 6. Forest plot of comparison: 14 HP strip versus CP tray, outcome: 14.1 Tooth whitening - assessed by the dentist.



Tooth whitening - assessed by the dentist

Among the 10 trials included in this group, seven trials used digital image analysis with CIEL*a*b* scoring (Gerlach 2000; Gerlach 2002b; Gerlach 2002a; Karpinia 2002; Ferrari 2007; Hannig 2007; Costa 2012). One trial (Botelho 2017) used a colorimeter with CIEL*a*b* scoring and two trials used the Vita shade guide (Kugel 2002; Li 2003).

Gerlach 2002b comparing 6% HP strips to 5% CP with desensitiser for 1 week, revealed 59% greater composite colour change for the strip group compared to the tray (MD -0.71, 95% CI -1.35 to -0.07; 1 trial, 32 participants; Analysis 14.1).

Gerlach 2000; Gerlach 2002a; Karpinia 2002; and Hannig 2007 compared similar concentrations of HP strips and 10% CP in tray and were combined in a meta-analysis. The combined analysis favoured the HP strip group in comparison to 10% CP in tray (MD -0.42, 95% CI -0.92 to 0.09; 4 trials, 149 participants; Analysis 14.1).

Li 2003 (who used 6.5% HP strips versus 16% CP in tray) favoured the tray group (MD 2.10, 95% CI 1.16 to 3.04; 1 trial, 55 participants; Analysis 14.1).

Ferrari 2007 at 6 weeks reported better whitening with HP strip group (L*) in comparison to 10% CP though the result was not statistically significant (MD -0.30, 95% CI -0.95 to 0.35; 1 study, 36 participants; Analysis 14.1). However, b values showed favourable results for the strip group at all intervals with statistical significance (P = 0.049).

Kugel 2002 reported that the 6.5% HP strip group experienced statistically significant superior reductions in shade compared to 10% CP in tray at both 1 and 2 month time points (2 months: MD -2.63, 95% CI -4.45 to -0.81; 1 trial, 33 participants; Analysis 14.1).

Intergroup comparison of 6.5% HP strips versus 15% CP in tray in Botelho 2017 showed that the tray group had greater overall colour changes (E) than the strip group at 3 months. However, no evidence of a difference was found between the groups at 3 months (MD 3.15, 95% CI -0.15 to 6.45; 1 trial, 24 participants; Analysis 14.1).

Twice daily use of 14% HP or 35% CP for 2 weeks in Costa 2012 split-mouth trial resulted in significant improvement in tooth lightness relative to baseline. However, no difference was seen between the groups at 2 weeks and 1 month interval (1 month: MD 0.58, 95% CI -0.61 to 1.77; 1 trial, 24 participants; Analysis 14.2).

Tooth whitening - reported by the patient

Costa 2012 used a patient satisfaction questionnaire to assess patient satisfaction of tooth whitening. 75% of participants could not see the difference in tooth whitening between the tray and strips. 255 of the patients who noted the difference felt the side that was whitened by the tray was whiter.

Hannig 2007 reported subjective colour score as reported by the patients. No difference between the groups was noted (MD -0.41, 95% CI -2.05 to 1.23; 1 trial, 43 participants; Analysis 14.3).

Patient comfort

Costa 2012 used the patient satisfaction questionnaire to assess patient comfort. 83% of participants in this split-mouth trial preferred the tray treatment to the strips. 75% found it more comfortable to the teeth and only 38% found it more comfortable to soft tissues. 92% of the patients reported that it was easy to do the procedure twice a day. Kugel 2002 reported that two patients in the 10% CP tray group dropped out from the study after 1 month due to inconvenient regimen.

Adverse effects

Tooth sensitivity and oral irritation were the most common adverse events. Gerlach 2005 reported sensitivity was more common with the 20% tray system. In one trial (Karpinia 2002) tooth sensitivity was more common in the strip group and oral irritation was common in the tray group. Some trials did not show any difference in adverse events between the two groups (Gerlach 2002a; Gerlach 2002b; Kugel 2002; Li 2003; Ferrari 2007; Hannig 2007; Costa 2012).

No other outcomes were reported.

2d. HP strips versus HP tray

Among the two trials in this comparison, Auschill 2012 used Vita shade guide and Gerlach 2004 used digital image analysis using CIEL*a*b* scoring.

Tooth whitening - assessed by the dentist

Gerlach 2004 which compared 14% HP strips and 9.5% HP in tray reported a superior 2-fold increase in lightness in the strip group at the end of treatment (22 days) compared to the tray group (MD -1.40, 95% CI -2.35 to -0.45; 1 trial, 29 participants; Analysis 15.1). However, initial whitening at 10 days did not differ between the groups.

Comparison of 5% HP strips to 5.3% HP gel in tray in Auschill 2012 showed no difference in whitening between the groups at 7 days, 2 weeks and 18 months intervals (18 months: MD 0.06, 95% CI -2.24 to 2.36; 1 trial, 28 participants; Analysis 15.1).

Patient comfort

One trial (Auschill 2012) reported patient acceptance graded based on VAS scale ranging from 0 to 10 (where 0 = no discomfort or best acceptance and 10 = severe discomfort or no acceptance). Statistical analysis of data demonstrated that the tray group showed statistically significantly more comfort (VAS 2.23 ± 1.49) than the strip group (VAS 3.50 ± 1.58) (MD 1.27, 95% CI 0.13 to 2.41; 1 study, 28 participants; Analysis 15.2).

Adverse effects

Tooth sensitivity and oral irritation were mild and transient and did not differ between the groups (Gerlach 2004; Auschill 2012).

No other outcomes were reported.

2e. HP strip versus HP strip

Tooth whitening - assessed by the dentist

Both trials (Shahidi 2005; Oliveira 2013) used digital image analysis with CIEL*a*b* scoring.

In Oliveira 2013 the 2-hour 9.5% HP high adhesion strips group demonstrated statistically significant lightness improvement (L*) than the 30 minutes 10% HP group on 3, 5 and 9 days (9 days: MD -1.50, 95% CI -2.33 to -0.67; 1 trial, 29 participants; Analysis 16.1).

Shahidi 2005 concluded that twice daily use of the very thin 10% HP gel strips resulted in significant tooth whitening after 7 days. Continued use of 10% strips at 15 days yielded significant incremental whitening greater than that seen with the lower concentration (6% HP strips) (MD 0.68, 95% CI 0.16 to 1.20; 1 trial, 35 participants; Analysis 16.1).

Adverse effects

Oliveira 2013 reported that nearly all adverse events were classified as mild in severity. Very thin gel group exhibited lower occurrence of oral irritation and higher tooth sensitivity compared to the 6% group (Shahidi 2005).

No other outcomes were reported.

2f. HP strip versus HP mouthwash

Tooth whitening - assessed by the dentist

Gerlach 2005 used digital image analysis with CIEL*a*b* scoring comparing HP pre-rinse to HP strips. Under the head-to-head testing conditions, 7-day use of 10% HP whitening strips resulted in significant tooth colour improvement relative to the 2% HP rinse (MD -1.10, 95% CI -1.49 to -0.71; 1 trial, 28 participants; Analysis 17.1).

Adverse effects

In Gerlach 2005 tooth sensitivity and oral irritation was more common in the strip group. All adverse events were mild in severity and no subjects discontinued treatment because of these events.

No other outcomes were reported.

2g. CP paint-on gel versus HP strips

Tooth whitening- assessed by the dentist

Two trials (Wong 2004; Cronin 2005) comparing 18% CP paint-on gel with 6% HP strips and using digital images with CIEL*a*b* scoring were combined in a meta-analysis. In both trials 6% HP strips were more effective in tooth whitening compared to the CP paint-on gel (SMD 1.50, 95% CI 1.06 to 1.94; 2 trials, 102 participants; Analysis 18.1).

Tooth whitening - reported by the patient

One trial (Wong 2004) reported patient satisfaction, rated using a product satisfaction questionnaire. Satisfaction regarding the whitening effect of the product was highest for the strip group (91%) compared to the paint-on group (33%).

Oral health-related quality of life

Wong 2004 reported the standardised response mean for the OHIP and its domains for subjects in each category of the global transition judgement on whether they were dissatisfied (-1), neutral (0) or satisfied (1). The authors felt that OHIP was not a suitable instrument to determine impact of tooth whitening on quality of life.

No other outcomes were reported.

2h. HP paint-on gel versus HP strips

Tooth whitening - assessed by the dentist

Two trials, Auschill 2007 using Vita shade guide and Xu 2007 using digital image analysis and CIEL*a*b* scoring showed that HP strips provided superior whitening compared to the paint-on gel group (Xu 2007: MD 1.28, 95% CI 0.77 to 1.79; 1 trial, 33 participants; Analysis 19.1); (Auschill 2007: MD 2.70, 95% CI 2.08 to 3.32; 1 trial, 40 participants; Analysis 19.2).

Tooth whitening - reported by the patient

One trial (Auschill 2007) reported no difference in patient satisfaction score between the 5.9% HP strip and paint-on groups (MD -0.25, 95% CI -1.88 to 1.38; 1 trial, 40 participants; Analysis 19.3).

Adverse effects

Xu 2007 reported that adverse events were mild in severity, and did not contribute to any treatment modification or early withdrawal. Auschill 2007 found a slightly higher tooth hypersensitivity and a slightly higher gingival irritation in the strip group although there was no evidence of a difference between the groups.

No other outcomes were reported.

2i. SPC paint-on versus HP strips

Tooth whitening - assessed by the dentist

Bizhang 2007 reported that the 6% HP strips yielded significant ($P < 0.02$) initial whitening relative to 19% sodium percarbonate (SPC) paint-on film when measured using digital image analysis and CIEL*a*b* scoring (MD 0.93, 95% CI 0.59 to 1.27; 1 trial, 47 participants; Analysis 20.1).

Adverse effects

Bizhang 2007 reported tooth sensitivity and oral irritation as the most common adverse events, with strip use. These adverse events were typically symptomatic only, and confined to the treatment period.

No other outcomes were reported.

2j. CP paint-on versus CP paint-on

Tooth whitening - assessed by the dentist

Two trials included in this comparison used Vita shade guide for measuring shade change.

Li 2004 trial used 18% CP with different application times. Between-group analyses at 7, 14 and 21 days showed the means for groups 3x (3 times a day) and 4x (4 times a day) to be significantly higher than 2x (twice a day) group. However, 3x and 4x groups did not differ significantly (7 days; 2x versus 4x: MD 1.39, 95% CI 0.50 to 2.28; 1 trial, 69 participants; Analysis 21.1).

Brunton 2004 comparing 18% and 16.4% CP found both groups with equally effective improvement in whiteness and the difference in whiteness between the two groups was neither statistically nor clinically significant (MD -0.70, 95% CI -2.21 to 0.81; 1 trial, 93 participants; Analysis 21.1).

Adverse effects

Li 2004 reported one subject to have very mild tooth sensitivity on the 7th day from the 4 times daily application group. Brunton 2004 reported that both gingival and tooth sensitivity were reported to be transient and caused none of the subjects to withdraw from the study.

No other outcomes were reported.

2k. CP paint-on versus HP paint-on

Tooth whitening - assessed by the dentist

Nathoo 2003 trial results indicated no evidence of a difference between 25% CP and 8.7% HP paint-on gels, though the shade improved in both groups compared to baseline measured according to the Vita shade scale (MD -0.16, 95% CI -1.39 to 1.07; 1 trial, 59 participants; Analysis 22.1).

No other outcomes were reported.

2l. HP paint-on versus HP-paint-on

Tooth whitening - assessed by the dentist

Ziebolz 2008 used Vita shade guide and reported significant improvement in tooth colour, in both groups compared to baseline. However no evidence of a difference was found between the groups (MD -0.10, 95% CI -0.56 to 0.36; 1 trial, 67 participants; Analysis 23.1).

Patient comfort

Ziebolz 2008 reported that in both groups similar proportion of the subjects reported lack of comfort. Comfort rating on a 4-point ordinal scale ranging from comfortable to very uncomfortable did not differ significantly.

No other outcomes were reported.

Adverse effects

Ziebolz 2008 reported tooth sensitivity in both groups with no evidence of a difference.

No other outcomes were reported.

2m. SPC paint-on versus CP paint-on

Tooth whitening - assessed by the dentist

Barlow 2003 who used digital image analysis with CIEL*a*b* scoring, showed significant and meaningful improvement in tooth colour in 19% sodium percarbonate group used overnight compared to 18% CP used twice daily for 7 days and 14 days (14 days: MD -0.58, 95% CI -0.95 to -0.21; 1 trial, 38 participants; Analysis 24.1).

Adverse effects

Barlow 2003 reported adverse events related to gum irritation and lip irritation. All events were mild and only one subject in the 18% CP group discontinued the treatment.

No other outcomes were reported.

2n. SPC paint-on versus HP paint-on

Tooth whitening - assessed by the dentist

Gerlach 2003 used digital image analysis with CIEL*a*b* scoring and reported uniform whitening for all individual and composite colour parameters for both 8.7% HP and 19% SPC groups. Head-to-head clinical testing of these two paint-on gels demonstrated 4-fold greater improvement in composite colour for the 19% SPC group (MD -0.36, 95% CI -0.71 to -0.01; 1 trial, 56 participants; Analysis 25.1).

Adverse effects

Gerlach 2003 reported tooth sensitivity in one subject from both groups. One subject in the 19% SPC film group reported oral sensitivity. All adverse events were symptomatic and mild in severity.

No other outcomes were reported.

DISCUSSION

Summary of main results

See Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5; Summary of findings 6; Summary of findings 7; Summary of findings 8; Summary of findings 9; Summary of findings 10; Summary of findings 11; Summary of findings 12; Summary of findings 13; Summary of findings 14; Summary of findings 15; Summary of findings 16; Summary of findings 17; Summary of findings 18; Summary of findings 19.

Bleaching agent versus placebo

Twenty-six trials compared different whitening products with placebo or no treatment.

Key results for this comparison have been discussed below independently for each outcome**.**

Key results for the outcome: tooth whitening - assessed by the dentist

Tray versus placebo: Summary of findings for the main comparison; Summary of findings 2

- Carbamide peroxide (CP) gel in tray at 5% and 10% concentrations with varying application times and duration, was more effective than the placebo gel (very low-certainty evidence).
- Hydrogen peroxide (HP) gel in tray at 3% and 6% concentrations applied twice daily for 2 weeks, was more effective than the placebo gel (very low-certainty evidence).

Strips versus placebo: Summary of findings 3

- HP strips at 5.3%, 6%, 10% and 14% concentrations, with varying application times were more effective than the placebo gel (low- and very low-certainty evidence).

Paint-on versus placebo: Summary of findings 4; Summary of findings 5

- CP paint-on gel at 18% concentration and HP paint-on gel at 6%, applied twice daily for 2 weeks, was more effective than the placebo gel (very low-certainty evidence).

Chewing gum versus placebo: Summary of findings 6; Summary of findings 7

- Sodium hexametaphosphate (SHMP) chewing gum at 4%, 5.6% and 7.5% concentrations, used 4 or 8 times a day showed reduction in stains compared to placebo gum (very low-certainty evidence).
- Sodium tripolyphosphate (STPP) chewing gum at 1% concentration used 3 times a day showed a reduction in stains compared to placebo gum (very low-certainty evidence).

Mouthrinse versus placebo: Summary of findings 8

- Fluoridated HP mouthwash, improved the shade of the teeth compared to placebo (very low-certainty evidence).

Key results for the outcome: tooth whitening - reported by the patient

- Patient satisfaction regarding bleaching reported in two trials comparing CP gel in tray to placebo and HP strips to placebo showed more satisfaction in the intervention group.

Key results for the outcome: patient comfort

- Patient comfort was more for the HP gel in tray group compared to HP strips.

Key results for the outcome: adverse effects

- Main adverse events reported in most trials were mild and transient tooth sensitivity and oral irritation, which occurred more in the intervention group compared to placebo. However, the placebo group in some trials (tray versus placebo) reported adverse events, which could be due to irritation from the tray.

Key results for the outcome: oral health-related quality of life

- Oral health-related quality of life (OHRQoL) reported in two trials comparing HP strips to placebo did not show any significant effect of tooth whitening on improvement in quality of life.

Bleaching agent versus bleaching agent

Fifty-one trials compared one bleaching agent to another bleaching agent.

Key results for this comparison have been discussed below independently for each outcome.

Key results for the outcome: tooth whitening - assessed by the dentist

Tray versus tray: Summary of findings 9; Summary of findings 10

- Overnight application of two different brands of 10% CP formulations showed no difference between Opalescence and Nite White (very low-certainty evidence). In another trial, Polanight was shown to have superior whitening compared to Opalescence (very low-certainty evidence). A single trial with 48 participants compared Colgate Platinum and Rembrandt Lighten and showed improved lightening in the CLP group.
- 10% CP in tray compared to 15% / 16% CP in tray favoured the higher concentration group irrespective of duration of use and application time (very low-certainty evidence). However, at the 2-year follow-up no evident difference was found between the groups.
- 10% CP with and without desensitisers (potassium nitrate and sodium fluoride) did not show any difference between the groups when used overnight for 2 weeks (very low-certainty evidence). However, 16% CP + amorphous calcium phosphate (ACP) showed better whitening when used for 3 hours a day for 2 weeks (low-certainty evidence).
- Overnight application of 5% and 10% concentrations of CP did not show any difference in whitening between the groups (very low-certainty evidence).
- Varying concentrations of HP and CP in tray did not show any significant difference at 2 weeks or 12 weeks duration (very low-certainty evidence). However, one trial showed superiority of 10% CP in tray over 6% HP in tray especially for the darkest shade teeth (very low-certainty evidence).

Strip versus tray: Summary of findings 11; Summary of findings 12

- 6% HP strip was more effective in whitening effect compared to 10% CP group when tested for a duration of 2 weeks (very low-certainty evidence). Similar concentrations tested at 6 weeks did not show any difference between the groups (very low-certainty evidence).
- 6.5% HP strips compared to 16% CP in tray favoured the CP tray group when tested at 21 days and 3 months duration (low-certainty evidence). However, one trial comparing 6.5% HP to 10% CP in tray tested for 2 months duration showed better whitening for the strip group.
- Twice daily application of 14% HP and 35% CP did not show any differences in the intergroup comparison (very low-certainty evidence).
- 6.5% HP strips compared to 15% CP did not show any difference between the groups (very low-certainty evidence).
- 6% HP strips showed greater composite colour scores when compared to 5% CP with desensitiser (very low-certainty evidence).
- 14% HP strips showed 2-fold increase in lightness compared to 9.5% HP in tray (very low-certainty evidence).
- 5% HP strips compared to 5.3% HP gel in tray showed no difference in whitening between groups (very low-certainty evidence).

Strip versus strip: Summary of findings 13

- 9.5% high adhesion HP strips were more effective compared to 10% HP strips applied for 30 minutes (very low-certainty evidence).
- 10% HP strips with a very thin gel were more effective compared to 6% HP strips (very low-certainty evidence).

Strip versus mouthwash

- 10% HP whitening strips resulted in significant whitening of teeth compared to 2% HP mouthrinse used twice daily.

Paint-on versus strips: Summary of findings 14; Summary of findings 15

- 6% or 5.9% HP strips showed more improvement in tooth whitening when compared to 18% CP or 5.9% HP paint-on gels with varying application times and duration (very low-certainty evidence). Similar results were obtained when HP strips were compared to 19% sodium percarbonate paint-on gel.

Paint-on versus paint-on: Summary of findings 16; Summary of findings 17; Summary of findings 18; Summary of findings 19

- No difference was found between 18% and 16.4% CP concentrations applied twice daily for 2 weeks (very low-certainty evidence).
- 18% CP application 4 times a day was more effective compared to 2 times application (very low-certainty evidence).
- 19% sodium percarbonate group was more effective in comparison to 18% CP used twice a day and 8.7% HP used overnight (very low-certainty evidence).
- HP paint-on with and without desensitiser did not show any difference in tooth whitening. However, these results are from a single trial and cannot be considered with certainty.

- No difference was found between 25% CP and 18.5% HP (very low-certainty evidence).

Key results for the outcome: tooth whitening - reported by the patient

- Patient contentment for 17% CP in tray and 10% CP in tray groups were similar with no significant difference (very low-certainty evidence).
- Patient-reported satisfaction was more for the 5% HP tray group compared to 5.3% HP strip group (very low-certainty evidence).
- No significant differences in patient satisfaction was observed for the paint-on and strip groups (very low-certainty evidence). Tooth hypersensitivity and oral irritation were more in the HP strip group with no statistical difference between the paint-on group comparators.

Key results for the outcome: patient comfort

- Patient comfort was better for the lower concentration group when CP in tray was tested against CP in tray.
- Patient comfort did not vary for 7.5% HP in tray and 10% CP in tray groups.
- Patient comfort was similar for 6% HP formulations with and without desensitiser. No significant difference was found in adverse events between any of the comparisons.

Key results for the outcome: adverse effects

- Higher concentrations of CP in tray led to more tooth sensitivity and gingival irritation. However, the symptoms were mild and transient. CP in tray with desensitiser showed significantly less sensitivity compared to the groups without the desensitiser. No difference was found between HP and CP in tray groups in relation to tooth sensitivity and oral irritation.
- When HP strips were compared to CP gel in tray, results were variable for adverse reactions (tooth sensitivity and oral irritation) with some trials favouring the strip group, some favouring the tray group and some showing no differences between the groups.
- When HP strips were compared to HP strips, very thin gel had lesser tooth sensitivity compared to thicker gel even though the concentration of HP was higher. Strips applied for 2 hours had greater symptoms of sensitivity compared with the 30-minute group. However, these results were not significant.
- Adverse events occurred more in the strip group compared to mouthwash but were not significant.

Key results for the outcome: oral health-related quality of life

- No difference in OHRQoL was found in 10% CP in tray compared to 16% CP in tray.

Overall completeness and applicability of evidence

Completeness

We systematically searched for trials according to the methodology written in the protocol. We did an independent Google search and checked all cross references of included articles and other systematic reviews on home-based bleaching to be sure that we did not miss any article. Two pairs of review authors did data extraction in duplicate. Trials, which were not included in the meta-analysis were explained qualitatively. We selected trials with adult participants needing tooth whitening and included all types of interventions with different application methods and concentrations. We included comparisons with placebo as well as head-to-head comparisons. All clinically relevant outcomes of interest were analysed. We also included trials in which staining of teeth was due to tetracycline staining and smoking.

We did not exclude any trial due to missing data. For trials reporting data in graphs, we derived the data by magnifying them and approximating the measures of mean and standard deviation. When mean and standard error (SE) were given, we calculated the standard deviation (SD) as given in the *Cochrane Handbook for Systematic Reviews of Interventions* section 7.7.3.3 (Higgins 2011). When adjusted mean was given, we considered it in the analysis (Higgins 2011, section 9.2.3.2). When median and interquartile range were given we used the data to calculate mean and SD. When mean and P value were given, SD was calculated. When data were presented as median (skewed data), we qualitatively described the results in the review. When data were presented as odds ratios, log (odds ratio) was calculated based on the odds ratios and 95% confidence intervals given in the trial and the generic inverse variance method was applied.

Applicability

Although we had 71 trials (78 reports) included in this review, most of the comparisons were single trials and could not be combined in meta-analyses due to varying methods of application, concentrations, application times, and duration of use. Bleaching agents in any mode of application were shown to be effective compared to placebo though the certainty of evidence is very low. The evidence generated is also of very low quality for most of the comparisons testing a bleaching agent versus another bleaching agent, and hence the results cannot be considered with certainty. Most of the trials report on short-term improvement of shade (ranging from 1 day to 1 month) using home bleaching methods. As follow-up has not been reported in most trials, the results cannot reflect the retention period for the whitening effect. However, the review encourages further high-quality randomised controlled trials (RCTs) to be conducted by standardising methods of application, concentrations, application times, and duration of application.

Quality of the evidence

The overall certainty of the evidence was low to very low for all comparisons. When a bleaching agent was compared to placebo for the first outcome looking into improvement of shade as measured by the dentist, except for 6% HP strips compared to placebo, for which evidence was of low certainty, all the other comparisons had a very low-certainty evidence. In the bleaching agent versus bleaching agent comparisons, the evidence for 16% CP in tray compared to 6.5% HP strip and 16% CP with amorphous calcium phosphate compared to 16% CP was graded as low certainty. The evidence from all remaining studies was graded as very low certainty. Three studies on patient contentment or satisfaction related to whitening treatment, which were included in the meta-analysis were graded as of very low-certainty evidence.

We downgraded the trials mainly for two reasons. Most of the trials were graded serious for risk of bias as they were at an unclear risk of bias and very serious to serious for imprecision as most of the trials were single with limited number of participants and low

event rates. Few trials that were combined in meta-analysis had high heterogeneity due to which we downgraded the certainty.

Potential biases in the review process

We have taken steps to minimise bias in every step of the review. We searched all the above mentioned databases, conference proceedings, and trial registries to include all relevant reports. We included foreign language reports in our review. We tried to contact trial authors for missing data through emails, peer contacts, Google search and university/hospital websites where they were previously affiliated. Nevertheless, there could be unpublished data which we could not trace with the above methods. We checked all cross-references in the included articles and other systematic reviews conducted on home-based bleaching and found articles which were missed in the search. Two review authors independently reviewed data extraction forms obtained from translators and cross-checked doubtful areas using the Google translator.

Agreements and disagreements with other studies or reviews

We found three systematic reviews on home-based bleaching and three conference abstracts.

Niederman 2000 studied only 10% CP tray-based bleaching products, published between 1989 and 1999 and concluded on the superiority of the intervention over placebo. All the included seven trials have been reported in our review and interpreted similarly.

Gerlach 2007 and Gerlach 2009 studied the efficacy and safety of HP whitening strips against placebo and other controls concluding that strips exhibited superior whitening. All the trials included in these systematic reviews are included in our review and were in agreement with the two systematic reviews.

Three conference abstracts were identified which were systematic reviews of home-based bleaching products. Brennan 2003 included trials with 19% sodium percarbonate and Gerlach 2013 did a meta-analysis of trials using 10% HP strips. Gerlach 2010 reported the analysis of peroxide-based self-directed products. We did not compare these with our review due to the lack of complete details.

This Cochrane Review had a broader focus and included all types of bleaching agents and different methods of application compared to the other systematic reviews reported.

AUTHORS' CONCLUSIONS

Implications for practice

We found low to very low-certainty evidence over short time periods to support the effectiveness of home-based chemically-induced bleaching methods compared to placebo for all the outcomes tested.

We were unable to draw any conclusions regarding the superiority of home-based bleaching compositions or any particular method of application or concentration or application time or duration of use, as the overall evidence generated was of very low certainty. Well-planned randomised controlled trials (RCTs) need to be conducted by standardising methods of application, concentrations, application times, and duration of treatment.

Implications for research

Further research should be undertaken to know the effectiveness of home-based bleaching methods by conducting well-planned RCTs with more clarity and uniformity in the variables. In designing such clinical trials, the following needs to be considered.

- Evidence: the present evidence was insufficient to conclude that any of the comparisons of home-based bleaching methods are effective. Trials should focus on testing similar concentrations with similar methods of application. Trials should focus on both short-term and long-term benefits of treatment. Studies should also focus on patient-related outcomes and cost effectiveness. Furthermore, reports on clinical trials would be improved by following CONSORT recommendations.
- Population: inclusion criteria for clinical trials should be well defined. Trials should include both genders in equal distribution.
- Intervention: intervention should focus on similar concentrations used in earlier studies and similar application times with a longer follow-up. This will add on to the existing evidence pool allowing us to make robust conclusions.
- Comparison: various comparisons have been reported, but we found only single trials in most of the comparisons due to which the quality of evidence is very low. Hence, RCTs need to be conducted keeping in mind already published studies so that the number of trials for a particular comparison increase.
- Outcome: patient-reported outcomes were not considered in most of the trials. Cost effectiveness also needs to be added in the RCTs, which is of most interest to consumers.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aka 2017

Methods	Title: evaluation of the efficacy and colour stability of 2 different at-home bleaching systems on teeth of different shades Trial design: randomised, parallel-group, controlled clinical trial Location: Izmir Katip Celebi University, Turkey Language: English Number of centres: 1 Recruitment period: January to July 2014 Funding source: not reported
Participants	Participants: 20 to 51 years old, mean age 26 years Total number: 200 Inclusion criteria: • good general health • adults 18+ • no caries or restoration on the teeth • permanent teeth • availability for follow-up • at least 1 front teeth from each shade category Exclusion criteria: • history of allergy • tetracycline stain • poor oral hygiene • pregnant or lactating women • having parafunctional habits • current or previous use of bleaching • orthodontic treatment • hypersensitivity Number randomised: 92 (all patients had similar number of light, medium dark and dark shaded teeth) Method of randomisation: randomisation table Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 90
Interventions	Total number of intervention groups: 3 Group 1: placebo n = 31 Group 2: 10% carbamide peroxide gel (Opalescence PF) n = 30 Group 3: 6% hydrogen peroxide gel (Opalescence Go) n = 31

Aka 2017 *(Continued)*

	Duration of treatment: 14 days Each group was further divided based on the shade **(tooth level analysis)** Control group: light teeth n = 90, medium dark teeth n = 91, dark teeth n= 93 Experiment Group 2: light teeth n = 89, medium dark n = 81, dark teeth n = 83 Experiment Group 3: light teeth n = 91, medium teeth n = 88, dark teeth n = 81
Outcomes	Shade evaluation (dental spectrophotometer); tooth sensitivity, gingival irritation and patient satisfaction (self-assessed using a 7-point scale: 1 correlating to no sensitivity, no problems, or no satisfaction; 7 correlating to severe sensitivity, problems, or satisfaction
Notes	Sample size calculation: given Adverse effects: tooth sensitivity and irritation Key conclusions of the study authors: "A pre-loaded tray system may be used for dental bleaching, but it is still less effective than conventional 10% carbamide peroxide system, irrespective of the initial shade. Bleaching was more effective with dark teeth compared to light teeth. Patient satisfaction was higher in 10% CP group compared to 6% HP" Correspondence required: no Contact: Department of Restorative Dentistry, Faculty of Dentistry, Izmir Katip Celebi University, Izmir, Turkey

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were randomly assigned to one of the two treatment groups and a control group using a randomization table…"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessed as at high risk of bias due to the lack of clarity of how teeth were selected for outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 patients from 6% HP/Go groups with 6 light shades of teeth did not attend the 6 months visit" Comment: Plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Alonso 2006

Methods	Title: comparison of the clinical efficacy and safety of carbamide peroxide and hydrogen peroxide in at-home bleaching gels Trial design: split-mouth randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 18 to 50 years, mean age: 31.8 years Total number: 16 Inclusion criteria: • subject availability to attend the control visits • good overall general health • a minimum of 24 natural teeth, including at least 4 molars (excluding third molars) • willingness to refrain from the use of any type of mouthrinse during participation in the study Exclusion criteria: • medication; need of antibiotic prophylactic therapy to receive dental treatment • smoking habit • pregnant or breastfeeding • presence of active cavities; anterior sector restorations covering > 1/6 of the labial surface • anterior teeth with root canal treatment • crowns or veneers on anterior teeth • a Löe-Silness Gingival Index 25 above 1 • stains confirmed to be due to tetracycline Number randomised: 16 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 16
Interventions	Total number of intervention groups: 2 3.5% hydrogen peroxide gel + 5% potassium nitrate 10% carbamide peroxide gel Duration of treatment: 3 hours a day on each arch, renew the gel every hour for 4 weeks
Outcomes	Change in tooth colour Vita shade guide: B1 lightest (1) – C4 darkest (16) Dental sensitivity: a scale of 4 levels, absence of sensitivity (grade 0), slight sensitivity not necessitating suspension of treatment (grade 1), sensitivity that forced suspension of treatment for 1 day (grade 2), sensitivity that led to suspension of treatment for more than 1 day (grade 3)

Alonso 2006 *(Continued)*

	Gingival irritation: present or absent
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Under the conditions of this study, no statistically significant differences were detected between 3.5% hydrogen peroxide containing 5% potassium nitrate (FKD) and the 10% carbamide peroxide-based product (Opalescence)" Correspondence required: no Contact: Victor Alonso de la Peña; victorap@mundo-r.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Both groups applied the products on a random basis"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 16 patients completed the study
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Alonso 2014

Methods	Title: randomised clinical trial on the efficacy and safety of 4 professional at home tooth whitening gels Trial design: randomised controlled clinical trial Location: Faculty of Medicine and Dentistry, Santiago de Compostela, Spain Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported

Alonso 2014 *(Continued)*

Participants	Participants: mean age 25.9 years Total number: 96 Inclusion criteria: • 18 years and older • minimum 24 natural teeth, with incisor, canine and premolars in both arches • absence of periodontal disease and gingival recession • availability to complete the study Exclusion criteria: • systemic illness • antibiotic prophylaxis • pregnant and breastfeeding women • tumours of hard and soft palate • presence of restoration • xerostomia, smokers • fluoride supplements and desensitizing agents • removable prosthesis • previous history of bleaching Number randomised: 96 Method of randomisation: based on alphabetical order Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 96
Interventions	Total number of intervention groups: 4 10% carbamide peroxide 15% carbamide peroxide 7.5% hydrogen peroxide 9.5% hydrogen peroxide Duration of treatment: 2 weeks
Outcomes	Change in colour Vita shade guide arranged from lightest to darkest B1 (1) to C4 (16). And change in score was recorded ΔL, a*, b* were recorded (b*: decreased b indicates reduced yellowness; ΔL: increased ΔL is increased brightness) Sensitivity: 0 = none, 1 = mild, 2 = moderate, 3 = considerable, 4 = severe
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported

Alonso 2014 *(Continued)*

Key conclusions of the study authors: "There were no differences in the degree of whitening among the different products. With all of the products there was an increase in L*, a decrease in chromatic intensity (C*), and an increase in the value (tone) or hue (h*)"

Contact: Dr Teijeiro; victorap@mundo-r.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...they were randomly divided into 4 groups of 24 individuals by alphabetical order"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "this was controlled, parallel, randomized one centre…" However, method of blinding is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "this was controlled, parallel, randomized one centre…" However, method of blinding is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 96 participants completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Auschill 2007

Methods	Title: a clinical comparison of 2 over-the-counter bleaching systems Trial design: examiner-blinded, split-mouth randomised controlled trial Location: Freiburg, Germany Language: German (translates to English using Google translate) Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 21 to 36 years old. Mean age: 25.5 years Total number: 26 Inclusion criteria: • A3 or darker shade • presence of anterior teeth to premolar

Auschill 2007 *(Continued)*

	Number randomised: 26 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 20
Interventions	Total number of intervention groups: 2 5.9% hydrogen peroxide gel 5.9% hydrogen peroxide strips Duration of treatment: 32 days
Outcomes	Improvement in tooth shade Vita shade guide: C1 lightest (1) to B4 darkest (16)
Notes	Sample size calculation: not reported Adverse effects: hypersensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The subjects teeth treated with the strips-system exhibited a 6.0 +/- 0.0 mean shade scores improvement compared to baseline (53.7 cycles; 1610.3 min), and the subjects teeth treated with the gel-system exhibited a 3.3 +/- 1.4 mean shade scores improvement (64.6 cycles; 969.0 min). However, both treatments were able to whiten teeth statistically significantly compared to baseline. Side effects caused by the 2 systems were minimal and reversible. None of the teeth studied showed detectible enamel surface changes in the subsequent SEM analysis. Both methods were well accepted" Contact: Thorsten.auschill@uniklini-freiburg.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote:"...subjects were randomly assigned to one of two groups." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not done
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Examiner-blinded split-mouth randomised controlled trial." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "6 out of 26 patients no longer appeared for follow-up" Comment: as each group had 20 participants (split-mouth trial) we rated it as low risk according to Higgins 2011 Section 8.5.d. Missing outcome data balanced in numbers across intervention groups

Auschill 2007 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Auschill 2012

Methods	Title: randomised clinical trial of the efficacy, tolerability, and long-term colour stability of 2 bleaching techniques: 18-month follow-up Trial design: 2-cell, parallel, examiner-blinded, randomised controlled trial Location: Albert-Ludwigs-University, Freiburg, Germany Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 56 years old, mean age: 33.08 years Total number: 30 Inclusion criteria: • maxillary central incisor with A3 or darker shade • free of restorations • no prior bleaching Exclusion criteria: • fixed orthodontic appliance • tooth hypersensitivity Number randomised: 30 Method of randomisation: a computer-based randomisation Method of allocation concealment: not reported Method of blinding: personal examiner blinding done by coding which was only known to statistician Number evaluated: 28. 2 dropouts at follow-up
Interventions	Total number of intervention groups: 2 Tray group: 5% hydrogen peroxide Strip group: 5.3% hydrogen peroxide Duration of treatment: 14 days
Outcomes	Improvement in tooth shade Vita shade guide: ranked from lightest B1 (1) to darkest C4 (16); mean score for anterior teeth was calculated Adverse effects. Patient recorded: mild, moderate and severe

Auschill 2012 *(Continued)*

	Patient acceptance, gingival irritation, sensitivity VAS scale: 0 (best acceptance) to 10 (no acceptance)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Key conclusions of the study authors: "Both bleaching techniques (the tray technique with 5.0% hydrogen peroxide and the strip technique with 5.3% hydrogen peroxide) demonstrated similar success. Although a significant relapse in tooth shade was observed over an 18-month post bleaching period, treated teeth were still significantly lighter compared to baseline. Adverse effects were minimal and reversible. Patient acceptance was statistically significantly higher in the tray group compared with the strip group" Correspondence required: no Contact: Dr Thorsten M Auschill; auschill@med.uni-marburg.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-based randomisation scheme (generated before starting the study) allocated patients…"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "2-cell, parallel, examiner-blinded, randomised controlled trial." However, method is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "..examiners, who were blinded to the treatment modality and period, subjectively measured.. Personal blinding done by coding which was only known to statistician"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 had to be classified as dropouts for that single visit. Thus, 28 subjects were available at the 18-month follow-up" Comment: as each group had 14 participants each we considered it as low risk according to Higgins 2011 Section 8.5.d. Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Barlow 2003

Methods	Title: clinical response of 2 brush-applied peroxide whitening systems Trial design: double-blinded, randomised, controlled, parallel-group trial Location: university Language: English

Barlow 2003 *(Continued)*

	Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 48 years old, mean age: 23 years Total number: 38 Inclusion criteria: • healthy adults who provided informed consent Exclusion criteria: • poor general and oral health • prior bleaching • patients with orthodontic appliances and restorations in their maxillary anterior teeth • patients with tooth sensitivity Number randomised: 38 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: similar packet kits Number evaluated: 38
Interventions	Total number of intervention groups: 2 18% carbamide peroxide 19% sodium percarbonate (2 brush-applied whitening kits) Duration of treatment: 14 days
Outcomes	Improvement in tooth colour b*: decreased b* indicates reduced yellowness ΔL: increased ΔL is increased brightness ΔW: negative ΔW indicates colour closer to white
Notes	Sample size calculation: not reported Adverse effects: sensitivity and gingival irritation Health-related quality of life: not reported Key conclusions of the study authors: "Crest Night Effect provided significant and meaningful improvement in colour after 14 days... Both products were tolerated" Correspondence required: no Contact: A Barlow; barlow.ap@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement

Barlow 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote:"double-blind, randomised, controlled, parallel-group clinical trial." However, method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants were supplied with blinded study kit boxes"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind, randomised, controlled, parallel-group clinical trial." However, method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts reported
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Berga-Caballero 2006

Methods	Title: at-home vital bleaching: a comparison of hydrogen peroxide and carbamide peroxide treatments Trial design: randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: age not reported Total number: 6 Inclusion criteria: not reported Exclusion criteria: not reported Number randomised: 6 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 6
Interventions	Total number of intervention groups: 2

Berga-Caballero 2006 *(Continued)*

	10% carbamide peroxide: 20 to 28 days 3.5% hydrogen peroxide: 28 days Duration of treatment: 20 to 28 days
Outcomes	Improvement in tooth shade
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "In carbamide peroxide group, the daily length of application was 2 hours. In the first case the treatment lasted for 24 days, there was no pre- or post-operative sensitivity and the tooth shade changed from A4 (canines) – A3.5 (incisors) to A2 (canines) – A1 (incisors). In hydrogen peroxide the duration of treatment was similar (28 days), no sensitivity was shown during treatment and the shade changed from A3.5 (canines) – A3 (incisors) to A1. Case 3 presented a change in shade from A4 (canines) – A3 (incisors) to A2 (canines) – A1 (incisors) after only 20 days; in this case the patient did mention slight sensitivity in the anterior mandibular teeth throughout the treatment" Correspondence required: no Contact: Professor Dr Forner Navarro; forner@uv.es

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomly assigned to the two treatment groups." However, the method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	All subjects completed the trial
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Biesbrock 2004

Methods	Title: a chewing gum containing 7.5% sodium hexametaphosphate inhibits stain deposition compared with a placebo chewing gum

Biesbrock 2004 *(Continued)*

	Trial design: cross-over randomised controlled trial Location: USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 70 years old. Mean age: 39.1 years Total number: 20 Inclusion criteria: • 16 natural teeth with minimum 7 anterior teeth Exclusion criteria: • previous history of hypersensitivity to test products • multiple restorations • fixed prosthesis • temporomandibular joint disfunction Number randomised: 19 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 18
Interventions	Total number of intervention groups: 2 (cross-over) 7.5% sodium hexametaphosphate chewing gum Placebo Duration of treatment: 2 weeks with 78 hours washout time
Outcomes	Improvement in tooth shade: reduction in stain ΔL, a*, b* values were recorded. Increase in L and reduction in b indicated whitening
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Sodium hexametaphosphate delivered from a chewing gum prevents dental stain formation and facilitates stain removal, which leads to a perceptible whitening benefit" Correspondence required: no Contact: Dr Aron RB, Procter and Gamble Company, Healthcare Research Center, Manson, Ohio, USA
Risk of bias	

Biesbrock 2004 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomly assigned to one of two treatment groups." However, method was not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Randomised, double-blinded cross-over trial." However, method was not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Randomised, double-blinded cross-over trial." However, method was not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 woman abandoned the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Bizhang 2007

Methods	Title: clinical trial of long-term colour stability of hydrogen peroxide strips and sodium percarbonate film Trial design: randomised, placebo-controlled trial Location: Berlin, Germany Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 18 to 60 years old, mean age: 30 years Total number: 72 Inclusion criteria: • healthy adults with at least 16 natural teeth including 4 maxillary incisors • tooth shade score of A2 Exclusion criteria: • prior bleaching history • current sensitivity • acute dental treatment needs

Bizhang 2007 *(Continued)*

	Number randomised: 72 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: blinded test kits Number evaluated: 70
Interventions	Total number of intervention groups: 3 6% hydrogen peroxide whitening strips 19% sodium percarbonate brush-applied gel that dries to a film Placebo brush-applied gel without peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade Tooth whitening was characterized by decreased b* (reduction in yellowness) and increased ΔL* (increased brightness)
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "6% hydrogen peroxide whitening strips yielded significant (P < 0.02) initial whitening relative to baseline, placebo and a 19% sodium percarbonate, brush-applied film. All treatments were well-tolerated, both peroxide-containing systems exhibited appreciable color retention throughout the 18-month post-treatment period, and here were no meaningful, persistent adverse events seen with long-term follow-up" Correspondence required: no Contact: Dr Mozhgan Bizhang; mozhgan.bizhang@med.uni-duesseldorf.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A total of 72 subjects from the greater Berlin metropolitan area were randomised equally to the strip, film and placebo groups." However, the method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Products were dispensed in a blinded subject kit box"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "With the examiners still blinded as to treatment, these subjects (strip and film groups) were evaluated at post-treatment months 12, 15, 16, and 18"

Bizhang 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "With respect to subject disposition, 71 subjects completed the end-of-treatment visit, and 70 (97%) completed the month 6 …" Comment: 2 dropouts were noted. Plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Botelho 2017

Methods	Title: a randomised controlled trial of home bleaching of tetracycline-stained teeth Trial design: randomised, examiner-blinded controlled trial Location: University of Hong Kong Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: tray group: mean age 28.7 years; strip group: mean age 30.4 years Total number: 36 Inclusion criteria: • tetracycline stained teeth • maxillary anterior teeth sound or minimally restored • able to attend 4-month review Exclusion criteria: • subjects under 18 • medically unfit • pregnant or lactating • uncontrolled oral disease or infection • history of tooth whitening treatment • smoker • allergy to hydrogen peroxide or carbamide peroxide Number randomised: 26 Method of randomisation: coin toss Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 24 (2 dropouts (1 for each group) at follow-up)
Interventions	Total number of intervention groups: 2

Botelho 2017 *(Continued)*

	Tray: 15% carbamide peroxide Strip: 6.5% hydrogen peroxide Duration of treatment: 3 months
Outcomes	Improvement in tooth colour a*, b* and ΔL were recorded Whitening benefit was represented by negative b* (yellowness reduction), and positive ΔL (increasing lightness)
Notes	Sample size calculation: done Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Both groups experienced noticeable and significant ΔL*a*b* improvement at the end of the trial in comparison to the baseline. Significant improvement was observed in the first month for the tray group and in the first 2 months for the strip group (P < 0.05). While greater lightness improvement was observed in the tray group over the strip group in the first month, the opposite was noticed in the second month. There was no difference between 2 groups at the end of this trial and no adverse reactions were observed" Correspondence required: no Contact: Dr Botelho MG; botelho@hku.hk

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomly assigned to either group….. tossing coin"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Participants were clinically review by one reviewer who was blinded to their treatment." However, method of blinding is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Participants were clinically review by one reviewer who was blinded to their treatment." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "..each group had 1 participant that did not attend 2 months review" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Browning 2008

Methods	Title: comparison of traditional and low sensitivity whiteners Trial design: double-blinded, placebo-controlled clinical trial Location: Department of Restorative Dentistry, Indiana University School of Dentistry, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: adults Total number: 91 Inclusion criteria: • adults with no significant medical problems • maxillary cuspids, lateral incisors and central incisors had to be shade A3 or darker Exclusion criteria: • active caries, defective restorations • untreated periodontal disease Number randomised: 91 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 91
Interventions	Total number of intervention groups: 5 Experimental 1: 10% carbamide peroxide Experimental 2: 10% carbamide peroxide, 3% potassium nitrate Experimental 3: 10% carbamide peroxide, 0.5% potassium nitrate Experimental 4: 10% carbamide peroxide, 0.5% potassium nitrate, 0.25% sodium fluoride Group 5: placebo Duration of treatment: 11 weeks
Outcomes	Change in tooth shade. Vita shade guide lightest C1 (16) to B4 (1)
Notes	Sample size calculation: not reported Adverse effects: tooth, hard and soft tissue sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Participants using one of the two whiteners with 0.5% potassium nitrate had sensitivity levels equivalent to those using the placebo. Relative to the whitening agent with no desensitising agent, the addition of 0.5% potassium nitrate resulted in a significant reduction in the number of days of sensitivity experienced by participants. When compared to the whitener without any potassium nitrate, the addition of 3% potassium nitrate did not result in a significant reduction

Browning 2008 *(Continued)*

	in the number of days of sensitivity. The addition of potassium nitrate did not result in any significant change in bleaching efficacy" Correspondence required: no Contact: William D Browning; lewis46@iupui.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "placebo-controlled, double-blind randomised clinical trial compared..." However, method not mentioned
Allocation concealment (selection bias)	Unclear risk	Method not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Neither the participant nor the operator was aware which material was received." However, method is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Neither the participant nor the operator was aware which material was received." However, method is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts are mentioned
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Bruhn 2012

Methods	Title: vital tooth whitening effects on oral health–related quality of life in older adults Trial design: single-blinded, randomised, pre–test, multiple post–test design Location: Hampton Roads area of Virginia, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 50 years old and above Total number: 62 Inclusion criteria: • 50 years old and older • good general health, possessing cognitive ability

Bruhn 2012 *(Continued)*

- physical dexterity to perform daily oral care
- have at least 8 natural anterior teeth free from composite restorations, crowns, veneers
- no full or partial dentures and endodontic treatment
- refrain from using any over–the–counter tooth whitening products for the duration of the study

Exclusion criteria:

- visible calculus deposits on labial or lingual surfaces of anterior teeth
- severe tooth sensitivity
- professional whitening within the past 3 years

Number randomised: 62

Method of randomisation: not reported

Method of allocation concealment: not reported

Method of blinding: participants were assigned a number after being randomly assigned to a group

Number evaluated: 53

Interventions	Total number of intervention groups: 2 Control: placebo Experimental: 14% hydrogen peroxide Duration of treatment: 3 weeks
Outcomes	Trubyte New Hue Vitality Scale: 12 shades numbered from 1 to 12, with 1 being the lightest and 12 being the darkest Tooth Colour Satisfaction Scale (TCSS): very satisfied (5 points), satisfied (4 points), neither satisfied nor dissatisfied (3 points), dissatisfied (2 points) and very dissatisfied (1 point) Oral Health Impact Profile (OHIP): 5-point Likert scale: very often (5 points), fairly often (4 points), occasionally (3 points), hardly ever (2 points), never (1 point) Additional Questions Survey (AQS): none (1 point), 1 to 2 (2 points), 3 to 4 (3 points), 5 to 6 (4 points) and 7 or more (5 points)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: reported Key conclusions of the study authors: "The older adults who whitened their teeth experienced an increased satisfaction with their tooth colour as evidenced by the TCSS. Tooth whitening was not associated with improvements in overall OHRQoL, or its functional factors, psychological disabilities, psychological discomforts, physical disabilities and social disabilities subscales. Tooth whitening did affect the handicap subscale, which demonstrated that persons who experienced tooth whitening were more willing to work due to a perceived increase in health. Tooth whitening did affect the physical pain subscale, which demonstrated a lower OHRQoL for participants. Older adults who whitened their teeth reported fewer social activities 3 months after the initial post–testing. Regression analysis relating tooth colour satisfaction with overall OHRQoL revealed a significant correlation between tooth colour satisfaction and overall OHIP for the experimental group" Correspondence required: no Contact: Ann M Bruhn; abruhn@odu.edu

Bruhn 2012 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "62 participants 50 years of age and older were enrolled and randomly assigned to 1 of 2 groups by research assistants." However, the method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Clinicians collecting data were unaware of participant group status, since the participants were assigned a number after being randomly assigned to"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "A total of 53 participants completed the study" Comment: 9 dropouts were noted. Reason for dropouts not mentioned
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Brunton 2004

Methods	Title: a 6-month study of 2 self-applied tooth whitening products containing carbamide peroxide Trial design: double-blinded, randomised, controlled, parallel-group clinical trial Location: not reported Language: English Number of centres: not reported Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 70 years old Total number: 95 Inclusion criteria: • male and female subjects ranging in age from 18 to 70 years inclusive • good general and oral health • all maxillary anterior teeth present • availability for the 6-month duration of the study • a minimum Vita shade of A3 on 1 or more upper central incisors Exclusion criteria:

Brunton 2004 *(Continued)*

- presence of orthodontic appliances or any anterior tooth with a prosthetic crown or veneer
- tumours or significant pathology of the soft or hard tissues of the oral cavity
- moderate or advanced periodontal disease, rampant caries or any condition that the dental examiner considered exclusionary from the study
- 5 or more carious lesions requiring immediate care
- participation in any other study within 30 days preceding the clinical study
- pregnant or lactating females
- a history of allergies to tooth whitening products, personal care consumer products or their ingredients
- restorations on the teeth to be scored

Number randomised: 95

Method of randomisation: not reported

Method of allocation concealment: not reported

Method of blinding: not reported

Number evaluated: 93, 2 dropouts

Interventions	Total number of intervention groups: 2 18% (Group 1) carbamide peroxide 16.4% (Group 2) carbamide peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade The shade guide was arranged with the 16-shade tabs in order from B1 (1) to C4 (16) Gingival score: Loë and Silness Gingival Index Gingival and teeth sensitivity score: 0 none - 5 severe
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Both products effectively whitened teeth with a treatment time of 2-weeks. The different concentrations tested were equally effective in improving whiteness. The whitening systems tested produced little tooth or gingival sensitivity. Some whitening benefit is sustained for at least 6 months after cessation of treatment" Correspondence required: no Contact: Paul A Brunton; paul.brunton@man.ac.uk

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned

Brunton 2004 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 subjects failed to complete the 2-week study (1 from each group) for reasons unrelated to the study" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Cibirka 1999

Methods	Title: clinical study of tooth shade lightening from dentist-supervised, patient-applied treatment with 2 10% carbamide peroxide gels Trial design: randomised double-blinded study Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Ultradent
Participants	Participants: 18 years old and above Total number: not reported Inclusion criteria: not reported Exclusion criteria: • persons with significant medical problems • pregnant or nursing women • persons with a history of vital bleaching • ongoing fixed orthodontic treatment Number randomised: not reported Method of randomisation: randomisation table Method of allocation concealment: not mentioned Method of blinding: not reported Number evaluated: 66
Interventions	Total number of intervention groups: 2

Cibirka 1999 *(Continued)*

	10% carbamide peroxide from 2 different brands Duration of treatment: 2 weeks
Outcomes	Change in tooth colour Evaluation of colour for the 6 maxillary anterior teeth was done using a Vita shade guide at baseline, 1, 2, and 4 weeks Vita shade guide arranged in the order of lightness: C1 (1) to B4 (16)
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "The test revealed no statistically significant difference between group for lightening the teeth. The colour change was still significant after 2 weeks without further bleaching activity. The baseline evaluation of the maxillary incisors and canines for all subjects, regardless of group, demonstrated a significant shade difference, with the canines being darker. This difference was not seen after 2 weeks of active bleaching or at the 4-week evaluation" Correspondence required: no Contact: Roman M Cibirka; rcibirka@mail.mcg.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A statistician created a randomization table for all subjects and maintained subject identification"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "..outside of the box and the individual syringes were labelled with the subject number"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised double-blinded study." However, the method is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of subjects randomised to both groups (n = 32 in both groups) explained in the methodology does not match the numbers shown in the table (n = 32 and n = 34)
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Collins 2004a

Methods	Title: clinical evaluation of a novel whitening gel, containing 6% hydrogen peroxide and a standard fluoride toothpaste Trial design: examiner-blinded, stratified, parallel-design clinical trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported
Participants	Participants: 18 to 63 years old. Mean age 39.45 years Total number: 128 Inclusion criteria: • in good general health and had a desire to lighten their upper and lower anterior teeth • pregnant or lactating women • subjects were required to have at least 4 upper anterior teeth and 4 lower incisors Exclusion criteria: • orthodontic bands • self-reported tooth hypersensitivity • crowns/veneers or visible cosmetic restorations • subjects with advanced periodontal disease • used mouthrinses for the treatment/control of a periodontal condition Number randomised: 128 Method of randomisation: stratified randomisation Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 117
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide paint-on gel Placebo: non-whitening toothpaste Duration of treatment: 2 weeks
Outcomes	Improvement in tooth colour Vita shade guide: C1: lightest (1 rank) – B4: darkest (16 rank)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The self-applied tooth-whitening gel containing 6% hydrogen peroxide has been shown to significantly improve the whiteness of teeth after 1 and 2 weeks of product use, compared to the baseline and the toothpaste only group"

Collins 2004a *(Continued)*

	Correspondence required: no Contact: Dr Luisa Collins; luisa.z.collins@unilever.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were stratified based on their gender and age and randomly assigned." However, the method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "examiner-blinded, stratified, parallel-design clinical trial." However, method is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "examiner-blinded, stratified, parallel-design clinical trial." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: ".. from the 11 subjects that failed to complete the clinical trial" Comment: missing of outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Costa 2012

Methods	Title: comparison of 2 at-home whitening products of similar peroxide concentration and different delivery methods Trial design: randomised, single-blinded, split-mouth design Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Ultradent
Participants	Participants: 21 to 75 years old Total number: 25 Inclusion criteria: • be at least 18 years old • willing to sign a consent form • willing to return for post-whitening evaluation

Costa 2012 *(Continued)*

- presence of all 6 maxillary teeth equal or darker than 1M2 VITA bleached guide in the value
- have no maxillary anterior teeth with more than 1/6 of the facial surface covered with a restoration

Exclusion criteria:

- history of any medical disease that may interfere with the study or require special consideration
- presence of gross pathology
- use of tobacco products during previous 30 days
- current or previous use of whitening agent
- Loë and Silness 29 gingival score > 1.0
- pregnant or lactating women
- tetracycline-stained teeth

Number randomised: 25

Method of randomisation: not reported

Method of allocation concealment: not reported

Method of blinding: not reported

Number evaluated: 24

Interventions	Total number of intervention groups: 2 35% carbamide peroxide 14% hydrogen peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade: a*. b* and L were recorded. Whitening benefit was represented by negative b (yellowness reduction), and positive ΔL (increasing lightness) Sensitivity: VAS scale: 1 no pain, 10 severe pain
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "There was no significant difference in tooth colour change between carbamide peroxide and hydrogen peroxide at either time point. By the end of the study no participants reported tooth and gingival sensitivity. Participants preferred CP over HP" Contact: Dr D Costa; dacostaj@ohsu.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised, single-blinded, split-mouth design clinical study." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "randomised, single-blinded, split-mouth design clinical study." However, method is not reported

Costa 2012 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised, single-blinded, split-mouth design clinical study." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 25 participants enrolled and 24 completed the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Cronin 2005

Methods	Title: comparison of 2 over-the-counter tooth whitening products using a novel system Trial design: observer-blinded, parallel-group randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: sponsored by Pfizer
Participants	Participants: 18 years old and above Total number: 60 Inclusion criteria: • A2 or darker on 2 or 4 incisors Exclusion criteria: • restoration covering more than 25% of the facial surface of maxillary anterior teeth • orthodontic bands • significant oral pathology • professionally whitened teeth in the last 6 months Number randomised: 60 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 59
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide

Cronin 2005 *(Continued)*

	18% carbamide peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade: shade assessment by VITAPAN C4 -1 to B1 – 16 ΔL, a*, b* were recorded (b: decreased b* indicates reduced yellowness; ΔL: increased ΔL is increased brightness)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Both the treatment showed significant improvement in tooth shade. 6% hydrogen peroxide showed better improvement when compared to carbamide peroxide" Correspondence required: no Contact: Martin J Cronin, Director Dental Research, New Institutional Service Co, Northfield, New Jersey, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Qualifying subjects were stratified and randomly assigned to 1 of the 2 test products." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "examiner-blinded, randomised, parallel-group study." However, method is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "examiner-blinded, randomised, parallel-group study." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Of 60 enrolled in study with 59 completing the study" Comment: plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Delgado 2007

Methods	Title: tooth-whitening efficacy of custom tray-delivered 9% hydrogen peroxide and 20% carbamide peroxide during daytime use: a 14-day clinical trial Trial design: double-blinded, randomised controlled clinical trial

Delgado 2007 *(Continued)*

	Location: University of Puerto Rico Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate
Participants	Participants: 25 to 64 years of age Total number: 46 Inclusion criteria: • healthy male and female subjects aged 21 to 68 years • availability for the 2 weeks duration of the study • minimum average Vita shade of A3 for all 6 maxillary anterior teeth • 6 natural maxillary anterior teeth must be present and free of large restorations or extrinsic stains covering more than 1/3 of the facial tooth surface or a maximum of 1 dental prosthetic crown/facial veneer Exclusion criteria: • presence of orthodontic appliances • presence of tumours or significant pathology of the soft or hard tissues of the oral cavity • presence of moderate or advanced periodontal disease (ADA III or IV) • presence of 5 or more carious lesions requiring immediate care • use of stain-inducing medications or oral use products 1 month prior to, or anytime during, the 2 weeks of the study • participation in any other clinical study or test panel in the last month • pregnant or lactating women • allergies to tooth whitening products, personal care consumer products, or their ingredients Number randomised: 46 Method of randomisation: random list Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 37
Interventions	Total number of intervention groups: 2 Group I: Colgate Visible White containing 9% hydrogen peroxide (9% HP) Group II: Opalescence containing 20% carbamide peroxide (20% CP) Duration of treatment: 30 minutes for 2 weeks
Outcomes	Improvement in tooth shade The shade guide tabs were arranged B1 to C4 representing the 1 to 16 scale
Notes	Sample size calculation: not reported Adverse effects: gingival irritation Health-related quality of life: not reported

Delgado 2007 *(Continued)*

	Key conclusions of the study authors: "Both 9% hydrogen peroxide and 20% carbamide peroxide products effectively whitened teeth after 5, 7 and 14 days of once-a day 30-minute applications. 9% hydrogen peroxide produced a statistically significant tooth shade improvement compared to the tooth whitening effect of 20% carbamide peroxide after 5 days of product use. Colgate Visible White 9% hydrogen peroxide and Opalescence (20% carbamide peroxide) had a similar whitening effect after 7 and 14 days of use. Both tooth whitening products tested produced little tooth sensitivity or gingival irritation"
	Contact: Evaristo Delgado; edelgadoc@yahoo.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were assigned following a random list to 1 of the 2 treatment groups"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "randomised, single-centre, parallel-group, double-blinded clinical trial." However, method is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised, single-centre, parallel-group, double-blinded clinical trial." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "9 dropouts noted" Comment: 7 failed to keep up with study visits. Unbalanced number in both groups (20% CP: n=16 and 9% HP: n = 21). We are not sure if plausible effect size (difference in means) among missing outcomes may have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Ferrari 2007

Methods	Title: daytime use of a custom bleaching tray or whitening strips: initial and sustained colour improvement Trial design: randomised, parallel, examiner-blinded study Location: Livorno, Italy Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 19 to 56 years old. Mean age 32.8 years

Ferrari 2007 *(Continued)*

	Total number: 43 Inclusion criteria: • 18 years of age and older • no history of tooth whitening • no current tooth sensitivity Exclusion criteria: not reported Number randomised: not reported Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: blinded kit boxes Number evaluated: 36
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide strips 10% carbamide peroxide tray Duration of treatment: 2 weeks
Outcomes	Colour improvement a*. b* and ΔL were recorded Whitening benefit was represented by negative b* (yellowness reduction), and positive ΔL (increasing lightness)
Notes	Adverse effects: tooth sensitivity and gingival irritation Health-related quality of life: not reported Key conclusions of the study authors: "The strip system yielded significant reduction in yellowness compared to the custom tray, at both end-of-treatment and post-treatment monitoring. Compared to Week 2, the strip group retained 89%-92% of the initial colour improvement at Week 6 (4 weeks post-treatment), while the tray group had 80%-90%. Both daytime treatments were well-tolerated, with minor tooth sensitivity and oral irritation representing the most common findings" Correspondence required: no Contact: Professor Dr Marco Ferrari; ferrarimar@unisi.it

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised, parallel, examiner-blinded study." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Because of the dissimilar delivery systems, test products were supplied in blinded kit boxes"

Ferrari 2007 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised, parallel, examiner-blinded study." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "6 subjects (4 in the strip group and 2 in the tray group) missed the 2-week visit, while 1 additional subject (in the tray group) missed the.." Comment: 7 dropouts were reported. HP strips group n = 17 and CP tray group n = 19. Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gallo 2009

Methods	Title: evaluation of 30% carbamide peroxide at-home bleaching gels with and without potassium nitrate Trial design: double-blinded, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dent Mat
Participants	Participants: adults Total number: 40 Inclusion criteria: • shade darker than B65 • no sensitive teeth • not used a bleaching material in 5 years • no restorations in their maxillary anterior teeth Exclusion criteria: • unable to meet the time requirements • reported cold-sensitive teeth • pregnant or nursing Number randomised: 40 Method of randomisation: not mentioned Method of allocation concealment: not mentioned Method of blinding: not reported Number evaluated: 40

Gallo 2009 *(Continued)*

Interventions	Total number of intervention groups: 2 30% carbamide peroxide with 5% potassium nitrate in tray 30% carbamide peroxide in tray Duration of treatment: 1 hour per day for 10 days
Outcomes	Change in tooth shade: Bioform Colour Ordered Shade Guide System: B85 darkest (1) to B59 lightest (24) Sensitivity of tooth: 0 to 10 scale (0: no pain, 10: severe) Gingival irritation: 0 normal, 1 mild, 2 moderate, 3 severe
Notes	Sample size calculation: not reported Adverse effects: sensitivity and gingiva irritation Health-related quality of life: not reported Key conclusions of the study authors: "30% carbamide bleaching gels effectively whiten teeth without causing a significant increase in tooth sensitivity or changes in gingival condition. Potassium nitrate has little effect in sensitivity when treatment time is short" Correspondence required: no Contact: Dr John Gallo; jgallo@lsuhsc.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "this double-blinded, randomised clinical study evaluated the effectiveness..." However, method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Neither subjects nor evaluators knew which bleaching gel (treatment A….. was used.." However, method of blinding not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Neither subjects nor evaluators knew which bleaching gel (treatment A….. was used.." However, method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No mention of dropouts
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Garcia-Godoy 2004

Methods	Title: placebo-controlled, 6-week clinical trial on the safety and efficacy of a low-gel, 14% hydrogen-peroxide whitening strip Trial design: parallel-group, double-blinded, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: consenting adults, mean age: 32.1 years Total number: 39 Inclusion criteria: • A2 or darker shade • healthy adults with no sensitivity Exclusion criteria: • previous bleaching • restoration Number randomised: 39 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 35. 4 dropouts, 2 from each group
Interventions	Total number of intervention groups: 2 Experiment: 14% hydrogen peroxide Control: placebo Duration of treatment: 3 weeks
Outcomes	Improvement in tooth colour b*: decreased b* indicates reduced yellowness ΔL: increased ΔL is increased brightness ΔW: negative W indicates colour closer to white
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "Twice-daily use of Crest Whitestrips Supreme resulted in a highly significant improvement in tooth colour after 3 weeks, with colour improvement continuing over 6 weeks"

Garcia-Godoy 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised double-blinded parallel-group clinical trial. Eligible subjects were randomised to a low gel 14% ...or placebo group." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "randomised double-blinded parallel-group clinical trial." However, method of blinding is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised double-blinded parallel-group clinical trial." However, method of blinding is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 subjects 1 in each group discontinued treatment because of a treatment related adverse event" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2000

Methods	Title: a randomised clinical trial comparing a novel 5.3% hydrogen peroxide whitening strip to 10%, 15%, and 20% carbamide peroxide tray-based bleaching system Trial design: randomised controlled, examiner-blinded, parallel-group clinical trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 24 to 57 years old. Mean age: 42.8 years Total number: 36 Inclusion criteria: • adults willing to whiten teeth Exclusion criteria: • previous report of sensitivity

Gerlach 2000 *(Continued)*

	• large restoration • history of tooth whitening Number randomised: 36 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 32
Interventions	Total number of intervention groups: 4 5.3% hydrogen peroxide strip 10% carbamide peroxide gel in tray 15% carbamide peroxide gel in tray 20% carbamide peroxide gel in tray Duration of treatment: 14 days, 2 hours per day
Outcomes	Improvement in tooth colour ΔL, a*, b* values were recorded. Increase in ΔL and reduction b* indicated whitening
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: ".. all groups experienced a greater than 1-unit mean improvement in all parameters relative to baseline. For the primary study variable, reduction of yellow (delta b*) outcomes after 14 hours of using the experimental strip were comparable to those observed with the 10% tray group after 28 hours of use. These 2 treatment groups did not differ statistically with respect to any of the colour measurements used in this study. For the tray groups, there was a reasonable dose relationship for the primary endpoint, delta b*, with the 15% and 20% tray groups averaging 17% and 68% improvements in yellow, respectively, over the 10% group. Except for the 20% carbamide peroxide system, where sensitivity was relatively common, all test products were well tolerated" Correspondence required: no Contact: Dr Robert W Gerlach, 8700 Mason Montgomery Road, Mason OH, 45040 8006 USA; gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised controlled, examiner-blinded, parallel group." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Not Mentioned

Gerlach 2000 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised controlled, examiner-blinded, parallel group." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "4 participants missed day 14" Comment: missing outcome data balanced in numbers across intervention groups (n = 9 in HP strip and n = 8 in CP tray group)
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2002

Methods	Title: initial colour change and colour retention with a hydrogen peroxide bleaching strip Trial design: randomised double-blinded design Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble. The authors are employees
Participants	Participants: 18 to 71 years old. Mean age: 40.9 years Total number: 57 Inclusion criteria: • 18 years and above • no history of bleaching, sensitivity or restorative dentistry Exclusion criteria: • dental prophylaxis in last 3 months Number randomised: 57 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: identically labelled and packaged, differing in appearance only as to a unique subject number Number evaluated: 52 completed study and 49 completed follow-up
Interventions	Total number of intervention groups: 2 Experiment: 5.3% hydrogen peroxide – Crest white strips Control: placebo strips

Gerlach 2002 *(Continued)*

	Duration of treatment: 2 weeks
Outcomes	Improvement in tooth colour b*: decreased b* indicates reduced yellowness ΔL: increased ΔL is increased brightness ΔE: overall whiteness
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and gingival irritation Health-related quality of life: not reported Key conclusions of the study authors: "Whitening strip group continuing to demonstrate improvements in tooth colour relative to baseline and placebo. Age was found to significantly contribute to initial colour improvement, with younger subjects experiencing a greater initial reduction in yellowness compared to older participants, but not to post-treatment colour retention. The whitening strips were well tolerated, with minor tooth sensitivity and oral irritation representing the most common findings during treatment. There were no persistent or new treatment-related adverse events during the 6-month monitoring" Contact: Dr Robert W Gerlach, 8700 Mason Montgomery Road, Mason OH, 45040 8006 USA; gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised double-blinded placebo-controlled study.. subjects were randomised to either the whitening strip or placebo strip groups." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "All products in this double-blinded clinical trial were identically labelled and packaged, differing in appearance only as to a unique subject number"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Of the 57 enrolled subjects, 52 completed bleaching treatment, while 49 completed the 6-month study" Comment: placebo group has 29 participants while hydrogen peroxide group has 23 participants. In spite of this difference, the results favour the intervention group. Hence we presume that plausible effect size (difference in means) among missing outcomes may not have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described are reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2002a

Methods	Title: comparative clinical efficacy of 2 professional bleaching systems Trial design: randomised, parallel, examiner-blinded clinical trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 22 to 59 years old, mean age 38.25 years Total number: 20 Inclusion criteria: no history of previous bleaching Exclusion criteria: not reported Number randomised: 20 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: uniquely numbered subject identification label Number evaluated: 20
Interventions	Total number of intervention groups: 2 (tray versus strip) Hydrogen peroxide 10%: 30 minutes twice daily Hydrogen peroxide 6.5% + carbamide peroxide 10%: 2 hours once daily Duration of treatment: 14 days
Outcomes	Improvement in tooth shade. Colour change (ΔL*, Δa*, and Δb*) was determined by comparing each post-treatment visit to baseline. Negative Δb* (reduction in yellowness) and positive ΔL* (increased brightness) were considered to be indicative of a whitening benefit
Notes	Sample size calculation: not reported Adverse effects: 1 patient had mild irritation at the tip of tongue in strip group Health-related quality of life: not reported Key conclusions of the study authors: "Under the conditions tested, this clinical trial demonstrates that the 14-contact-hour treatment with the strip system resulted in superior whitening efficacy compared with the 28-contact-hour treatment with the tray system" Contact: Dr Robert W Gerlach; gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement

Gerlach 2002a *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "randomised, examiner-blinded, clinical trial." However, method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Test products were over labelled with a uniquely numbered subject identification label"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised, examiner-blinded, clinical trial." However, method is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 20 subjects completed the 14- day treatment and were considered eligible for evaluation for all analyses"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2002b

Methods	Title: comparative response of whitening strips to a low peroxide and potassium nitrate bleaching gel Trial design: randomised, examiner-blinded clinical trial. 2 arms Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: mean age of 37 years Total number: 34 Inclusion criteria: be willing to have their teeth whitened Exclusion criteria: • patients who has undergone bleaching or restoration of the maxillary anterior dentition • patients with ongoing tooth sensitivity Number randomised: 34 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not repeated

Gerlach 2002b *(Continued)*

	Number evaluated: 32
Interventions	Total number of intervention groups: 2 5% carbamide peroxide bleaching gel + potassium nitrate in custom tray: once daily application 6% hydrogen peroxide bleaching strip: twice daily application Duration of treatment: 7 days
Outcomes	Improvement in tooth shade ΔL, a*, b* were recorded. Increase in ΔL and decrease in b* indicates whitening
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "Twice daily application of 6% hydrogen peroxide strip resulted in better whitening compared to 1 daily application of 5% carbamide peroxide. Sensitivity was less with 6% hydrogen peroxide" Contact: gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Study subjects were randomly assigned to 1 of 2 groups." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "randomised examiner-blinded clinical study." However, method is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised examiner-blinded clinical study." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 subjects missed the day 7 visit" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2003

Methods	Title: randomised clinical trial comparing overnight use of 2 self-directed peroxide tooth whiteners

Gerlach 2003 *(Continued)*

	Trial design: blinded randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: mean age 40.3 years Total number: 57 Inclusion criteria: • A2 or darker Exclusion criteria: • prior bleaching • sensitivity in tooth • extensive restorative or orthodontic treatment Number randomised: 57 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: test products were over packaged in kit boxes that were labelled only with a unique subject identification number to assure blinding Number evaluated: 56, 1 dropout
Interventions	Total number of intervention groups: 2 Crest Night Effects 19% sodium percarbonate Colgate Simply White Night 8.7% hydrogen peroxide Duration of treatment: 14 nights
Outcomes	Improvement in tooth colour b*: decreased b* indicates reduced yellowness ΔL: increased ΔL is increased brightness ΔW: negative ΔW indicates colour closer to white
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "After 14 nights treatment, adjusted mean (SE) change in yellowness (delta b*) was -0.95 (0.092) for the 19% sodium percarbonate film and -0.17 (0.096) for the 8.7% hydrogen peroxide gel, with these groups differing statistically ($P < 0.0001$). Other individual and composite colour parameters also demonstrated significantly greater whitening for the 19% sodium percarbonate film compared to the 8.7% hydrogen peroxide gel after 14 nights use. Only the 19% sodium percarbonate film exhibited significant ($P < 0.0001$) proximal colour improvement (delta b*) after 2 weeks,

Gerlach 2003 *(Continued)*

approximately 98% of that seen on the body of the tooth, providing evidence of proximal bleaching and uniform spatial whitening following use of this barrier-free system. Both products were well-tolerated, with no subjects discontinuing treatment early due to a causal adverse event

PMID: 15055983

Contact: Dr Robert W Gerlach, Procter and Gamble Company, 8700 Mason Montgomery Road, Mason OH 45040 8006 USA; gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Blinded randomised controlled trial." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Method not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Test products were over packaged in kit boxes that were labelled only with a unique subject identification number to assure blinding"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 subject discontinued the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2004

Methods	Title: clinical trial comparing 2 daytime hydrogen-peroxide professional vital-bleaching systems Trial design: randomised, examiner-blinded clinical trial Location: USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: adults aged 18 to 64 Total number: 31 Inclusion criteria:

Gerlach 2004 *(Continued)*

	• healthy adults aged 18 or older who have 3 or more maxillary anterior teeth with a tooth shade of A2 or darker, as measured by using a standard 16-tab system Exclusion criteria: • prosthetic or orthodontic appliances on the maxillary dentition, dentine hypersensitivity, or a history of vital bleaching Number randomised: 31 Method of randomisation: not reported Method of allocation concealment: unclear Method of blinding: unclear Number evaluated: 29
Interventions	Total number of intervention groups: 2. 14% hydrogen peroxide whitening strips 9.5% hydrogen peroxide custom-tray–based system Duration of treatment: 22 days
Outcomes	Improvement in tooth colour: ΔL, a*, b* values were recorded. Increase in L and reduction b* indicated whitening
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritations were the most common side effects. 28% of the patients reported 1 or both. Occurrence of either sensitivity or irritation was 13% in strip group, 56% in tray group Health-related quality of life: not reported Key conclusions of the study authors: "At the end of the treatment, the 14% hydrogen peroxide whitening strips caused 2-fold reduction in yellowness and better in-use tolerability when compared to 9.5% hydrogen peroxide custom-tray system" Correspondence required: no Contact: gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomised, examiner-blinded clinical trial..." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "... which had been packed into a blinded kit box labelled with a unique subject number"
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "The randomised, examiner-blinded clinical trial..." However, method of blinding is not mentioned

Gerlach 2004 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 subject in each group did not return for the Day 22 visit" Comment: plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2004e

Methods	Title: placebo-controlled clinical trial evaluating a 10% hydrogen peroxide whitening strip Trial design: randomised, double-blinded, placebo-controlled trial Location: University of Florida, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 50 years old. Mean age: 38.8 years Total number: 39 Inclusion criteria: • no history of bleaching • no restorations • no orthodontic brackets • no tooth sensitivity Exclusion criteria: not reported Number randomised: 39 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: similar white foil packing with unique ID Number evaluated: 34. 2 dropouts on 8th day of evaluation and 3 for all parts of study
Interventions	Total number of intervention groups: 2 10% hydrogen peroxide whitening strips Placebo Duration of treatment: 7 days
Outcomes	Improvement in tooth colour

Gerlach 2004e *(Continued)*

	b*: decreased b* indicates reduced yellowness ΔL: increased ΔL is increased brightness
Notes	Sample size calculation: not reported Adverse effects: oral irritation and tooth sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Statistically significant tooth whitening was evident after 3 days' treatment with 10% hydrogen peroxide whitening strips, and colour improved with continued usage over 7 days" Contact: Dr Robert W Gerlach; gerlach.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A randomised double-blinded, placebo-controlled clinical trial was conducted... Groups were randomly assigned to treatment based on age and baseline tooth colour." No further details are given
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Each strip was packaged in an individual white foil pouch, with the subject identification number... Strips were over packaged in a kit box,.."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "3 subjects (1 in the 10% group and 2 in placebo group) failed all or pat of the day 8 evaluation" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes mentioned are reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Gerlach 2005

Methods	Title: clinical trial comparing 2 hydrogen peroxide tooth whitening systems: strips versus pre-rinse Trial design: randomised, examiner-blinded, parallel-group trial Location: not reported Language: English Number of centres: 1

Gerlach 2005 *(Continued)*

	Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 29 to 58 years old. Mean age 39.8 years Total number: 28 Inclusion criteria: • 4 maxillary anterior teeth • no sensitivity Exclusion criteria: not reported Number randomised: 28 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 28
Interventions	Total number of intervention groups: 2 Mouthwash: 2% hydrogen peroxide Strip: 10% hydrogen peroxide Duration of treatment: 7 days
Outcomes	Improvement in tooth shade a*, b* and ΔL were recorded Whitening benefit was represented by negative b* (yellowness reduction), and positive ΔL (increasing lightness)
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "Relative to baseline, the whitening strip group experienced colour improvement at day 3, continuing through day 8. The pre-rinse group did not show any significant change at day 3, and had a significant increase in yellowness at day 8. The strip group exhibiting significantly greater whitening at day 8. Both products were well tolerated, with no participants discontinuing treatment early as the result of an adverse event. In head-to-head testing, 7-day use of the 10% hydrogen peroxide whitening strips resulted in significant tooth colour improvement relative to a barrier-free 2% hydrogen peroxide pre-brushing mouthrinse" Correspondence required: no Contact: Dr Geralch; geralch.rw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement

Gerlach 2005 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "...subjects were randomly assigned to 1 of 2 test groups." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Examiner-blinded, parallel-group, randomised controlled trial." However, method of blinding not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Examiner-blinded, parallel-group, randomised controlled trial." However, method of blinding not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All the participants completed all the visits and were evaluated"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Giniger 2005

Methods	Title: a 180-day clinical investigation of the tooth whitening efficacy of a bleaching gel with added amorphous calcium phosphate Trial design: double-blinded randomised controlled trial Location: USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Discus Dental, Culver City, USA
Participants	Participants: continuation of a previously published study, 27 agreed to continue. Mean age 46.4 years Total number: 27 Inclusion criteria: • absence of severe systemic diseases • psychological diseases or both • maxillary anterior tooth discolouration (equivalent to or darker than Vita shade A3) • non-use of any dentist-supplied or -applied vital tooth bleaching treatment in the previous 6 months • non-user of any in-office desensitising agent in the previous 6-month period • no periodontal surgery or scaling performed in the previous 6 months • patients with no carious, non-restored 6 max anterior teeth Exclusion criteria: not reported Number randomised: 27

Giniger 2005 *(Continued)*

	Method of randomisation: stratified randomisation schedule Method of allocation concealment: secret coding Method of blinding: identical pack Number evaluated: 27
Interventions	Number of groups: 2 Control: 16% carbamide peroxide Experimental: 16% carbamide peroxide with 0.5% soluble calcium phosphate derived in part from calcium nitrate and potassium pyrophosphate Duration of treatment: 19 days
Outcomes	Improvement in tooth shade: Vita shade guide C1 (1) to B4 (16) Gingival Index score: 0 (no gingivitis) to 3 (severe gingivitis) Dentinal hypersensitivity: 0 (no pain) to 3 (pain during application of stimuli and immediately there after) VAS scale: 0 (no pain) to 10 (highest level of pain)
Notes	Adverse effects: none Key conclusions of the study authors: "This study demonstrated that the ACP product offers 10% better long-term (6-months) whitening efficacy that the traditional bleaching gel. No significant adverse effect. Tooth sensitivity, soft tissue health, and gingival health remained similar to baseline levels" Contact: Dr Giniger; mginiger@mg-co.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: " ..we randomised subjects into test and control groups, according to a stratified randomisation schedule"
Allocation concealment (selection bias)	Low risk	Quote: "The evaluator of the teeth shades and sensitivity scores (MG) was blinded to this schedule.. other than a secret product code number known only to a co-worker"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The evaluator of the teeth shades and sensitivity scores (MG) was blinded to this schedule, and the products looked identical to him and to the subjects"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The evaluator of the teeth shades and sensitivity scores (MG) was blinded to this schedule, and the products looked identical to him and to the subjects"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 27 requalified subjects completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results

Giniger 2005 *(Continued)*

Other bias	Low risk	None

Hannig 2007

Methods	Title: efficacy and tolerability of 2 home bleaching systems having different peroxide delivery Trial design: randomised, single-blinded, parallel-group trial Location: University of Göttingen, Germany Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 60 years. Mean age 29.35 years Total number: 47 Inclusion criteria: • volunteers with resorted or caries-free teeth • anterior tooth colour Vita shade A2 or darker • with no crowns on upper cupids or incisors Exclusion criteria: • patients with prior tooth sensitivity • restoration on anterior teeth • poor oral hygiene • generalized gingival recession • caries • heavy structural alteration of the tooth structure • tetracycline or fluorosis staining • patients with systemic disorders Number randomised: 47 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 43 (at 2 weeks)
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide strips 10% carbamide peroxide gel in tray Duration of treatment: 14 days
Outcomes	Tooth shade improvement: ΔL, a*, b* values were recorded. Increase in L and reduction on b*

Hannig 2007 *(Continued)*

	Patient satisfaction: to 10 (0 = no whitening, 10 = maximal satisfying whitening effect)
Notes	Sample size calculation: not reported Adverse effects: transient tooth sensitivity and oral soft tissue irritation Health-related quality of life: not reported Key conclusions of the study authors: "Both whitening systems showed significant tooth colour improvement after 2 weeks of use.... No statistical significant difference was observed between the 2 systems..... Both systems were well tolerated and caused comparable levels of transient tooth sensitivity and oral soft tissue irritation" Correspondence required: no Contact: Christian Hannig, christian.hannig@uniklinik-feriburg.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "this single-blinded, randomised, parallel-group study..... Subjects were stratified according to the baseline anterior maxillary tooth brightness (L*) as determined by digital image analysis system and by the criteria of smoker/non-smoker. Randomisation to treatment was performed within each strata." However, method not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "this single-blinded, randomised, parallel-group study." However, method not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "this single-blinded, randomised, parallel-group study." However, method not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "5 subjects dropped out of the study due to reasons not related to bleaching therapy at different stages. 2 subjects from the WS [strips] group withdrew after 5 days of treatment because of product-related side effects" Comment: number of participants at 2 weeks: 22 in tray group and 21 in strip group. Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Hasturk 2004

Methods	Title: efficacy of a fluoridated hydrogen peroxide-based mouthrinse for the treatment of gingivitis Trial design: randomised, double-blinded, placebo-controlled, parallel-group trial Location: Boston Medical Center, USA

Hasturk 2004 *(Continued)*

	Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dent Mat
Participants	Participants: 18 to 50 years old Total number: 110 Inclusion criteria: • had a minimum 20 natural teeth excluding wisdom teeth • no periodontitis or history of periodontitis • had natural anterior maxillary teeth with no restorations Exclusion criteria: • subjects who had orthodontic appliances • tumour in the oral cavity • carious lesions requiring immediate treatment • subjects who received antibiotic therapy in the 30 days before the study begins • subjects who were on long-term anti-inflammatory therapy Number randomised: 99 Method of randomisation: random numbers chart Method of allocation concealment: reported Method of blinding: similar coded bottle Number evaluated: 78
Interventions	Total number of intervention groups: 2 Hydrogen peroxide + 0.05% sodium fluoride mouthrinse Placebo Duration of treatment: 30 seconds twice daily for 6 months
Outcomes	Plaque Index Modified Gingival Index Bleeding on probing dichotomous (1 or 0) Intensity of stain: dichotomous (1 if lightened or if no change)
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Subjects using the test rinse were also 6 times more likely to exhibit an improvement in tooth colour after 6 months than were subjects using placebo. As a result of the clinical evaluations and microbial analysis, test mouthrinse was found to be safe during a 6-month period"

Hasturk 2004 *(Continued)*

Contact: Thomas E Van Dyke, tvandyke@bu.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Treatment was assigned by use of random number charts, and subject assignment was made by an individual who was not involved in the treatment or measurement procedures"
Allocation concealment (selection bias)	Low risk	Quote: "Treatment was assigned by use of random number charts, and subject assignment was made by an individual who was not involved in the treatment or measurement procedures"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quotes: "The placebo rinse was an identical base formulation to the test mouthrinse...;" " Mouthrinses were labelled to conform with prescribing regulations and were coded to maintain double masking ..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All clinical measurements were performed under the same conditions by the same investigator who was blinded to the treatment"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quotes: "Each subject was considered as the unit of analysis. Therefore, subject who completed at least 1 post-baseline clinical assessment visit were included in the intent-to-treat population;" "99 subjects were randomised, and 78 subjects completed the whole course of the study. 38 subjects were in placebo group and 40 in the test group" Comment: no details of reasons for dropouts are given
Selective reporting (reporting bias)	Low risk	All outcomes have been reported adequately. Conclusions conform to the results obtained
Other bias	Low risk	None

Hyland 2015

Methods	Title: a new 3-component formulation for the efficient whitening of teeth (Carbamide Plus) Trial design: randomised, double-blinded, placebo-controlled, clinical trial Location: Eastman Dental Hospital, UK Language: English Number of centres: 1 Recruitment period: not reported Funding source: SMT Ltd and DEL CAST studentship
Participants	Participants: adults Total number: 33 Inclusion criteria: not reported Exclusion criteria:

Hyland 2015 *(Continued)*

- heavily restored upper left central incisor or upper right canine
- pregnancy or breastfeeding
- previously undergone a course of vital tooth whitening
- smokers
- active dental disease
- severe dentine hypersensitivity
- uncontrolled dental disease
- unable to attend on data collection

Number randomised: 32

Method of randomisation: not reported

Method of allocation concealment: not reported

Method of blinding: not reported

Number evaluated: 32

Interventions	Total number of intervention groups: 3 5% carbamide peroxide gel 10% carbamide peroxide gel Placebo Duration of treatment: 2 hours per day for 2 weeks
Outcomes	Improvement in tooth colour ΔL, a*, b*: increase in ΔL and reduction in b* indicates whitening
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "A new tooth-whitening product Carbamide Plus containing urea, hydrogen peroxide, and STPP as active components containing 5% hydrogen peroxide has been shown to be as effective as the commercially available carbamide peroxide containing 10% hydrogen peroxide. There were no statistically significant differences between Carbamide Plus and 10% carbamide peroxide in tooth whitening at 2 weeks following daily wear of tooth whitening trays for 2 hours per day" Correspondence required: no Contact: BW Hyland; j.callan@ulster.ac.uk

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The recruited subjects were randomly allocated to 1 of 3 study groupings: non-active placebo gel..." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned

Hyland 2015 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "randomised, double-blinded, placebo-controlled clinical trial." However, method is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised, double-blinded, placebo-controlled clinical trial." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Karpinia 2002

Methods	Title: vital bleaching with 2 at-home professional systems Trial design: randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 65 years old. Mean age 37.2 years Total number: 69 Inclusion criteria: • 18 years and above • 4 maxillary anterior teeth with shade greater than A2 Exclusion criteria: • previous history of bleaching • sensitivity of the tooth Number randomised: 69 Method of randomisation: randomised in blocks of 4 Method of allocation concealment: not reported Method of blinding: unique coded label Number evaluated: 67
Interventions	Total number of intervention groups: 2

Karpinia 2002 *(Continued)*

	6.5% hydrogen peroxide strips 10% carbamide peroxide in tray Duration of treatment: 30 minutes twice daily for 3 weeks
Outcomes	Improvement in tooth shade: ΔL, a*, b* values were recorded. Increase in ΔL and decrease in b* indicates whitening
Notes	Sample size calculation: not reported Adverse effects: oral and gingival irritation Health-related quality of life: not reported Key conclusions of the study authors: "For between group comparisons, strip subjects had a statistically significant or directionally favourable whitening response relative to the tray system at intermediary time points, while at the end of treatment, the strip group had highly statistically significant (P < or = 0.005), superior whitening response for all colour parameters measured in the study. Both treatments were generally well tolerated, with 35% to 40% of the subjects in each group reporting minor tooth sensitivity or gingival irritation" Correspondence required: no Contact: KA Karpinia, University of Florida, Gainesville, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The study population was randomised in blocks of 4"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Each product was over labelled with a unique subject identification number"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 patients from tray group and 1 patient from tray and strip group missed the evaluation group at 7 days and 3 weeks respectively" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Kihn 2000

Methods	Title: a clinical evaluation of 10% versus 15% carbamide peroxide tooth whitening agents Trial design: randomised, double-blinded study Location: University of Maryland Dental School, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dentsply
Participants	Participants: 18 to 65 years old Total number: 57 Inclusion criteria: maxillary anterior teeth of shade A3 or darker Exclusion criteria: not reported Number randomised: 56 Method of randomisation: reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 52
Interventions	Total number of intervention groups: 2 Experiment: 15% carbamide peroxide gel Control: 10% carbamide peroxide gel Duration of treatment: 2 weeks
Outcomes	Improvement in tooth colour Sensitivity: 0 (no pain) to 20 (severe)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "There was a significant difference in colour change between the 10% CP and 15% CP groups at the end of the study period. There was no significant difference in level of tooth sensitivity between the 2 groups, and the incidence was equal; there was, however, a significant difference in variability of tooth sensitivity between the 2 groups" Correspondence required: no Contact: Patricia W Kihn; tkihn@caulk.com

Risk of bias

Bias	Authors' judgement	Support for judgement

Kihn 2000 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "paired list of names was supplied to the manufacturer, which then randomly assigned 1 member of each pair"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "authors conducted a double-blinded study of human subjects to..." However, method of blinding is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "authors conducted a double-blinded study of human subjects to..." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Of the 56 subjects who began the study, 26 pairs of matched subjects (n = 52 individual subjects) completed the study" Commnet: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Kose 2011

Methods	Title: clinical effects of at-home bleaching along with desensitizing agent application Trial design: randomised, double-blinded, controlled trial Location: University Estadua, Brazil Language: English Number of centres: 1 Recruitment period: not reported Funding source: FGM Dental Products
Participants	Participants: 18 to 30 years old. Mean age 24 years Total number: 60 Inclusion criteria: • 18 and older • 6 caries and restoration free teeth • A2 shade or darker Exclusion criteria: • previous vital bleaching, apparent caries, periodontal disease • orthodontic appliances, anterior restorations • history of dentine hypersensitivity • bruxism Number randomised: 60

Kose 2011 *(Continued)*

	Method of randomisation: coin toss Method of allocation concealment: not reported Method of blinding: similar syringes Number evaluated: 60
Interventions	Total number of intervention groups: 2 16% carbamide peroxide in tray + placebo 16% carbamide peroxide in tray + desensitizer gel (DG; 5% potassium nitrate and 2% sodium fluoride) Duration of treatment: 4 weeks
Outcomes	Improvement in tooth shade: Vita shade guide B1 (highest) to C4 (lowest) Tooth sensitivity: 0 - none, 1 – mild, 2 - moderate, 3 - considerable, 4 - severe
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The use of desensitizing agent did not affect the bleaching efficacy of the CP. The prevalence and intensity of tooth sensitivity was similar for both groups. However, participants from the placebo group had sensitivity in 33.6% of the bleaching days, which was significantly higher than the desensitizing agent experimental group (20.1%)" Correspondence required: no Contact: Dr Kose, School of Dentistry, State University of Ponda, Santa Catarina, Brazil

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "subjects were randomly divided into experimental or control group by coin toss"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither the subjects nor the evaluators knew to which group the subjects were assigned"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Neither the subjects nor the evaluators knew to which group the subjects were assigned"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 60 participants who began study completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results

Kose 2011 *(Continued)*

Other bias	Low risk	None

Kowitz 1994

Methods	Title: comparative clinical evaluation of 2 professional tooth whitening products Trial design: single-blinded, parallel, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: adults Total number: 50 Inclusion criteria: not reported Exclusion criteria: not reported Number randomised: 50 Method of randomisation: not reported Method of allocation concealment: reported Method of blinding: coded packs Number evaluated: 48
Interventions	Total number of intervention groups: 2 10% urea peroxide from 2 different brands 1 hour application twice daily Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade Sensitivity Patient-reported satisfaction
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Colgate Platinum was 62% more effective at tooth whitening after 1 week and 83% more effective after 2 weeks of treatment versus Rembrandt. At the termination of the study, the mean colour difference (deltaE) for Colgate Platinum was 4.29 and 2.34 for Rembrandt. Statistical analysis demonstrated that the Colgate product is significantly superior at increasing tooth whiteness, increasing tooth lightness, reducing redness, and reducing yellowness. In this study, no adverse reactions were noted on clinical examination and none were reported by panelists with normal healthy dentition"

Kowitz 1994 *(Continued)*

	Correspondence required: no Contact: Dr Kowitz, University of California, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "single-blinded, randomised, 2-celled parallel clinical trial." However, method of randomisation is not reported
Allocation concealment (selection bias)	Low risk	Quote: "Neither the subject no the investigator were informed to which group the individual belonged"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Each subject was assigned a coded test product...."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "2 dropped out because of problems unrelated to study" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Krause 2008

Methods	Title: subjective intensities of pain and contentment with treatment outcomes during tray bleaching of vital teeth employing different carbamide peroxide concentrations Trial design: double-blinded, randomised controlled trial Location: university Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: mean age 31 years Total number: 30 Inclusion criteria: • patients with teeth not discoloured for extrinsic or intrinsic reasons • non-smokers

Krause 2008 *(Continued)*

	Exclusion criteria: not reported Number randomised: 30 Method of randomisation: computer generated numbers Method of allocation concealment: not reported Method of blinding: unlabelled similar packs Number evaluated: 30
Interventions	Total number of intervention groups: 3 10% carbamide peroxide tray 17% carbamide peroxide tray 0% carbamide peroxide tray Duration of treatment: 7 days
Outcomes	Pain sensation Patient contentment with bleaching: 0 no contentment, 100 maximum contentment
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: yes, patient satisfaction Key conclusions of the study authors: "Application of carbamide peroxide–containing bleaching agents to vital teeth causes pain correlated with the agent's concentration. Since both highly and less concentrated gels might result in a similar contentment with the treatment outcome, the use of highly concentrated agents appears not to be justified to improve vital tooth colour" Contact: Felix Krause, fkrause@uni-bonn.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "kits were assigned to the patients employing computer-generated random numbers by a different operator"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Unlabelled treatment kits numbered consecutively. Thus, both the operator and the patient were unaware of the..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Unlabelled treatment kits numbered consecutively. Thus, both the operator and the patient were unaware of the..."
Incomplete outcome data (attrition bias)	Low risk	All participants completed the study

Krause 2008 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Kugel 2000

Methods	Title: tooth-whitening efficacy and safety: a randomised and controlled clinical trial Trial design: randomised, single-centre, double-blinded, parallel-group, placebo-controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 66 years old. Mean age 33 years Total number: 70 Inclusion criteria: • 16 natural teeth and minimum 4 anterior teeth • A2 shade or darker Exclusion criteria: • periodontal disease • tetracycline stains • restoration • dental caries • dental hypersensitivity • previous history of bleaching Number randomised: 70 Method of randomisation: block randomisation Method of allocation concealment: not reported Method of blinding: identical package and examiners were blinded Number evaluated: 66. 4 dropouts
Interventions	Total number of intervention groups: 2 5.3% hydrogen peroxide gel delivered with polyethylene gel Placebo Duration of treatment: 2 weeks
Outcomes	Change in tooth shade: Vita shade guide tabs arranged according to lightness (B1 light to C4 dark)

Kugel 2000 *(Continued)*

	Oral soft and hard tissue examination
	Dental hypersensitivity
	Gingival Index: Loë and Silness Index
	Plaque Index: Silness and Loë Index
Notes	Sample size calculation: not reported
	Adverse effects: soft tissue irritation and dental hypersensitivity
	Health-related quality of life: not reported
	Key conclusions of the study: "Peroxide gel-treated group showed significant whitening of teeth. Both treatments were generally well tolerated. The strips offer ease of use, comfort, and shorter duration of wear compared with other at-home bleaching systems"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The study was a randomised, placebo-controlled, double-blinded, parallel-group study. Block randomisation was done"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Except for the presence of peroxide, test products were identical in composition and packaging"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All examinations were performed blinded as to treatment assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 dropouts in each group at the end of the 2-week trial. It is unlikely that 4 dropouts could affect the overall results. Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes discussed were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Kugel 2002

Methods	Title: daily use of whitening strips on tetracycline-stained teeth: comparative results after 2 months
	Trial design: randomised controlled trial
	Location: Tufts University, USA
	Language: English
	Number of centres: 1
	Recruitment period: not reported

Kugel 2002 *(Continued)*

	Funding source: Procter & Gamble
Participants	Participants: 22 to 70 years old Total number: 40 Inclusion criteria: adult patients with tetracycline stains Exclusion criteria: not reported Number randomised: 40 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: identical packages Number evaluated: 33
Interventions	Total number of intervention groups: 2 6.5% hydrogen peroxide strips 10% carbamide peroxide tray Duration of treatment: 2 months
Outcomes	Improvement with tooth shade. Vita shade guide arranged from darkest to lightest (B4 to C1) Plus 2 additional shades of B4+ and C1+
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "6.5% carbamide peroxide strips provided similar benefit to 10% carbamide peroxide used over 2 months period" Correspondence required: no

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomised clinical trial." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Products were packed in 1 month kits, and all labelling was identical except for unique.."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned

Kugel 2002 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "7 subjects withdrew from the treatment in the first month" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Li 2003

Methods	Title: comparison of clinical efficacy and safety of 3 professional at-home tooth whitening systems Trial design: randomised, 3-cell, parallel-group, investigator-blinded trial Location: university Language: English Number of centres: 1 Recruitment period: not reported Funding source: Discuss Dental
Participants	Participants: 23 to 67 years old Total number: 90 Inclusion criteria: • all subjects had a minimum 20 natural teeth, including at least 4 maxillary incisors with a shade at or darker A3 Exclusion criteria: not reported Number randomised: not reported Method of randomisation: randomisation scheme generated by a computer Method of allocation concealment: reported Method of blinding: reported Number evaluated: 82
Interventions	Total number of intervention groups: 3 groups 6.5% hydrogen peroxide: 21 days, twice daily - 30-minute application 7.5% hydrogen peroxide: 18 days, twice daily - 30-minute application 16% carbamide peroxide: 21 days, overnight - 30-minute application Duration of treatment: 18 to 21 days based on the intervention
Outcomes	Improvement in tooth shade: Vitapan shade guide: B1 to C4 (lightest to darkest shade ranking) ΔL, a*, b* and ΔW using chromometre. Increase in L and W indicated whitening. Reduction in b* indicated whitening

Li 2003 *(Continued)*

Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "All 3 systems were effective and safe. Nite White Excel (16% CP) resulted in significant greater shade reductions in periods between days 7, 14, or 21 and baseline than did the other 2 systems. Tooth sensitivity and gingival irritation was seen in all groups, but it was lower in the Nite White Excel group" Correspondence required: no

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Qualified subjects were divided into ….. using randomisation scheme generated by computer"
Allocation concealment (selection bias)	Low risk	Quote: "To ensure blinding, the group assignment and product distribution was done by project coordinator who was not involved in the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "To ensure blinding, the group assignment and product distribution was done by project coordinator who was not involved in the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "To ensure blinding, the group assignment and product distribution was done by project coordinator who was not involved in the study... while clinical examiner performed examination without knowledge of treatment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 5 subjects withdrew….3 did not show up.." Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Li 2004

Methods	Title: comparative tooth whitening efficacy of 18% carbamide peroxide liquid gel using 3 different regimens Trial design: stratified, double-blinded, parallel-group, randomised controlled trial Location: Loma Linda University, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Pamolive

Li 2004 *(Continued)*

Participants	Participants: 18 to 65 years old. Mean age 39.06 years Total number: 120 Inclusion criteria: • all maxillary and anterior teeth present • teeth required to have a minimum A3 or darker shade on Vitapan • pregnant, lactating Exclusion criteria: • with orthodontic appliances, crowns, tumours, periodontal disease Number randomised: 120 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 104. 16 dropouts
Interventions	Total number of intervention groups: 3 18% carbamide peroxide: • 2x: twice daily, no air drying and 15 minutes without eating/drinking • 3x: 3 times daily, 30-second air drying and 30 minutes without eating/drinking • 4x: 4 times daily, 30-second air drying and 30 minutes without eating/drinking Duration of treatment: 21 days
Outcomes	Improvement in tooth shade Vita shade guide: lightest (C1) 1 to darkest (B4) 16 Oral tissue: normal/abnormal Gingival Index: Loë and Silness Gingival Index: 0 absence of inflation, 1 mild, 2 moderate, 3 severe Tooth sensitivity: 0 (no pain) to 10 (severe pain) Opinion survey: 1 (more positive) to 5 (least positive)
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: reported Key conclusions of the study authors: "Subjects who used 3x and 4x regimen achieved the greatest shade improvement. However those values were only 1 shade better than twice daily and no dry regimen. There was no significant difference between 3x and 4x regimens. Patients who used 2x and 3x regimens found it to be more convenient" Correspondence required: no Contact: Dr Yun Po Zhang; yun_zhzng@copal.com
Risk of bias	

Li 2004 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "120 qualifying subjects…. randomly assigned within strata to 1 of the 3..." However, the method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "stratified, double-blinded, parallel-group, randomised controlled trial." However, the method of blinding is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "stratified, double-blinded, parallel-group, randomised controlled trial." However, the method of blinding is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "104 subjects completed the clinical study: there were 16 dropouts…. The data revealed the number was well balanced" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Matis 1998

Methods	Title: efficacy and safety of a 10% carbamide peroxide bleaching gel Trial design: double-blinded, randomised controlled trial Location: Indiana University, School of Detitistry, Indianapolis, Indiana, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: mean age 45.27 years Total number: 60 Inclusion criteria: • no soft or hard tissue pathosis (excluding small carious lesions and mild gingivitis) • all 6 maxillary anterior teeth, with no more than 1/6 of the facial surface restored • non-smokers Exclusion criteria: • Loë and Silness Gingival Index (GT) > 1 Number randomised: 60

Matis 1998 *(Continued)*

	Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: dental assistant managed the grouping. All products were in identical syringes Number evaluated: 59. 1 patient dropped out from 4th week from active group
Interventions	Total number of intervention groups: 2 groups 10% carbamide peroxide gel in tray Placebo Duration of treatment: 2 weeks
Outcomes	Change in tooth colour: Truebyte shade guide: 0 lightest, 25 darkest Colourimetre: b*: decreased b* indicates reduced yellowness, L: increased L is increased brightness Gingival sensitivity Tooth sensitivity Gastrointestinal sensitivity Sensitivity scale: scale of 1 to 5: 1 = no sensitivity, 2 = slight sensitivity, 3 = moderate sensitivity, 4 = considerable sensitivity, 5 = severe sensitivity
Notes	Sample size calculation: not reported Adverse effects: gingival, tooth and gastrointestinal sensitivity was reported Health-related quality of life: not reported Key conclusions of the study authors: "The product used in this study is an effective and physiologically acceptable tooth whitening agent. Initial colour regression occurred within the first month for incisors, and within 10 weeks for canines, but neither regressed back to baseline for the duration of this 6- month study" Contact: Dr BA Matis; bmatis@iusd.iupui.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "60 patients were randomised into 2 equal subgroups balanced by age, gender, and oral health status." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Patients were given coded packages of Opalescence whitening gel. All products were in identical syringes"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A dental assistant was responsible for group balancing, so that the evaluators could continue to be blind to which treatment group each patient was assigned"

Matis 1998 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	At 2 weeks all 60 participants who were randomised were evaluated. However 1 dropout was noticed after 4 weeks and 22 weeks reporting. Plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described are reported adequately. Conclusions are in accordance with the results
Other bias	Low risk	None

Matis 2000

Methods	Title: clinical evaluation of bleaching agents of different concentrations Trial design: split-mouth, randomised controlled trial Location: Indiana University-Purdue University, Indianapolis, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Ultradent
Participants	Participants: 26 to 73 years old. Mean age 50.4 years Total number: 25 Inclusion criteria: • all 6 maxillary anterior teeth had to be present • none of the maxillary anterior teeth have more than 1/6 of its labial restoration • at least 18 years old • willing to refrain from the use of tobacco products during the study period Exclusion criteria: • use of professionally-applied or prescribed tooth whiteners, in-office bleaching, or mouthguard vital bleaching in the past 3 years • incisors or canines lighter than B54 or darker than B85 on the Trubyte Bioforin Colour Ordered Shade Guide (Dentsply) • gross pathosis in oral cavity (excluding caries) • Loë and Silness Gingival Index score > 1 • pregnancy or lactation • teeth discoloured by tetracycline staining Number randomised: 25 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 25
Interventions	Total number of intervention groups: 2

Matis 2000 *(Continued)*

	10% carbamide peroxide 15% carbamide peroxide with 0.11% fluoride ion Duration of treatment: 14 days
Outcomes	Whitening of tooth. ΔL, a*, b*. Increase in ΔL and reduction in b* indicated whitening
Notes	Sample size calculation: not reported Adverse effects: tooth and gingival irritation Key conclusions of the study authors: "All 3 methods of evaluation revealed a significant difference in the tooth lightness achieved by 10% and 15% products at 2 weeks but no significant difference at 6 weeks. No statistically significant difference was found in gingival or tooth sensitivity" Correspondence required: no Contact: Dr Bruce A Matis; Bmatis@ijsd.njpui.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This was a double-blinded, 6-week study in which participants were randomised into 2 groups by tooth shades." However, method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "This was a double-blinded, 6-week study in which participants were randomised into 2 groups by tooth shades." However, method is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "This was a double-blinded, 6-week study in which participants were randomised into 2 groups by tooth shades." However, method is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 25 subjects completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Matis 2006

Methods	Title: extended bleaching of tetracycline-stained teeth: a 5-year study Trial design: split-mouth, randomised controlled trial Location: Wuhan University School of Stomatology, China Language: English

Matis 2006 *(Continued)*

	Number of centres: 1 Recruitment period: not reported Funding source: Ultradent
Participants	Participants: not reported Total number: 59 Inclusion criteria: • 18 years of age • willing to sign a consent form • willing to return for periodic evaluations • willing to refrain from tobacco use for first 9 months of study • presence of 6 maxillary anterior teeth • no more than 1/6 of the facial surface of above teeth covered with restoration • presence of tetracycline staining Exclusion criteria: • use of bleaching agents in past 3 years • use of tobacco during previous 30 days • Loë and Silness gingival score > 1 • study teeth lighter than A3 • history of disease that would interfere with study • presence of gross pathology • pregnant or lactating Number randomised: 59 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 44
Interventions	Total number of intervention groups: 3 10% carbamide peroxide 15% carbamide peroxide 20% carbamide peroxide Duration of treatment: 6 months
Outcomes	Improvement in tooth colour: colourimeter readings in CIELa*b* for Vitalescence Restorative Masters Shade Guide
Notes	Sample size calculation: not reported Adverse effects: tooth and gingival sensitivity Key conclusions of the study authors: "The maximum lightening that occurred within 6 months happened during the first month of bleaching. Values increased the most during the bleaching of tetracycline stained teeth. There were small changes in the green red or blue-yellow spectrums of colour throughout the study. At 4.5 years post-bleaching, all 3 concentrations of bleaching agents had re-

Matis 2006 *(Continued)*

	tained more than 65% of their original colour change. Increased tooth sensitivity occurs with higher concentrations of CP gels"
	Correspondence required: no
	Contact: Dr Bruce A Matis; Bmatis@ijsd.njpui.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "At baseline evaluation, subjects were randomly assigned to 1 of 6 groups." However, method is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Subjects were not aware of the concentration of bleaching agent they were using." However, method is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Of the 59 subjects who initially enrolled in the study, 44 completed the 5-year evaluation. Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Mederios 2008

Methods	Title: effectiveness of nightguard vital bleaching with 10% carbamide peroxide
	Trial design: randomised controlled trial
	Location: Universidade Federal do Rio Grande do Norte, Brazil
	Language: English
	Number of centres: 1
	Recruitment period: not reported
	Funding source: not reported
Participants	Participants: university students. 18 to 25 years old. Mean age 21.6 years
	Total number: 50
	Inclusion criteria: • central and lateral upper incisors and had no fillings • tooth sensitivity

Mederios 2008 *(Continued)*

- endodontic treatment
- previous tooth bleaching
- periodontally healthy teeth
- non-smokers

Exclusion criteria: not reported

Number randomised: 50

Method of randomisation: raffle

Method of allocation concealment: not reported. Patients were randomly allotted to either group

Method of blinding: the placebo was placed in empty Opalescence PF packaging so that neither the volunteer nor the examiner knew which gel was being used

Number evaluated: 49

Interventions	Total number of intervention groups: 2 10% carbamide peroxide gel in tray Placebo Duration of treatment: 21 days
Outcomes	Change in tooth shade: Vita shade guide - arranged from lightest to dark (1 light and 16 darkest) Gingival Bleeding Index modified by Lang Tooth sensitivity: yes or no Patient satisfaction: satisfactory or non-satisfactory
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and gingival bleeding Health-related quality of life: reported Key conclusions of the study authors: "NGVB with 10% carbamide peroxide, when use in the current study, was effective for lightening tooth colour, both for the period immediately after treatment and for the 6-month follow-up period. Of the 2 main side effects assessed, tooth sensitivity was more prevalent than gingival irritation" Contact: Dr Medeiros; cristinamedeiros@digizap.com.br

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "In a simple raffle, the 50 volunteers were randomly allocated to 1 of the 2 groups.."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The placebo gel had the same physical characteristics as the experimental gel. The placebo was placed in empty Opalescence PF packaging so that neither the volunteer nor the examiner knew which gel was being used"

Mederios 2008 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All analysis were done by the evaluator" Comment: but it is not mentioned whether the same evaluator dispensed the gel or not
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All volunteers completed the study.... The data of 1 volunteer from the placebo group were lost because of upper right lateral incisor anodontia" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described are reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Meireles 2010

Methods	Title: double-blinded randomised clinical trial of 2 carbamide peroxide tooth bleaching agents: 2-year follow-up Trial design: double-blinded, randomised clinical trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: not reported Total number: 183 Inclusion criteria: • 6 anterior maxillary teeth with a colour shade C1 or darker • evaluated teeth should not have more than 1/6 of the buccal surface restored, and the restoration should not interfere with the spectrophotometer readings • volunteers should have good oral health (no dental caries and periodontal disease) • good general health (no disease that could interfere with the study results) • volunteers should be at least 18 years old Exclusion criteria: • volunteers under orthodontic treatment or with tetracycline stained teeth • volunteers reporting past or present hypersensitivity or those having non-vital anterior teeth • volunteers that used tooth whiteners within the past 3 years • smokers, pregnant or lactating women • volunteers without schedule availability Number randomised: 92 Method of randomisation: randomisation table Method of allocation concealment: not reported

Meireles 2010 *(Continued)*

	Method of blinding: labels were removed Number evaluated: 91
Interventions	Total number of intervention groups: 2 Control: carbamide peroxide 10% in tray Experimental: carbamide peroxide 16% in tray Duration of treatment: 2 hours per day for 3 weeks
Outcomes	Improvement in tooth shade: ΔL, a*, b* values recorded Oral impact on daily performance (OIDP) 0 = no sensitivity; 1 = mild sensitivity; 2 = moderate sensitivity; 3 = considerable sensitivity and 4 = severe sensitivity The self-reported general health was based on a Likert scale: excellent; very good; good; regular; bad (latter categorized in excellent/very good and good/regular)
Notes	Sample size calculation: mentioned Adverse effects: tooth sensitivity Health-related quality of life: reported Key conclusions of the study authors: "The whitening effect evaluated by visual shade matching and digital spectrophotometer remained similar after 6 months of bleaching treatment using any of the carbamide peroxide concentrations tested. Additionally, the high consumption of staining beverage and food had no influence in the whitening effect longevity. Quality of life is complex and encompasses different domains. Although positive impact of the dental bleaching was detected, with patients showing more their teeth without embarrassment, difficult in dental hygiene and pain resulting from the treatment were also reported, and this can negatively impact daily performances. Dentists must consider these aspects when performing aesthetics procedures" This is a 2-year follow-up report of the previous study Correspondence required: no Contact: SS Meireles; soniasaeger@hotmail.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomisation table to allocate the participants in each study...."
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The product concentration label was removed, therefore, the examiners and participants were blinded to the agent"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned

Meireles 2010 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	1 dropout. Plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Mohan 2008

Methods	Title: clinical study to evaluate the efficacy of a novel tray-based tooth whitening system Trial design: parallel, examiner-blinded, stratified, randomised controlled trial Location: Department of Fixed and Removable Prosthodontics, Leeds Dental Institute, UK Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 18 to 70 years old Total number: 50 Inclusion criteria: • available for the 2-week duration • minimum of 20 uncrowned teeth with at least 6 upper front teeth without crowns or large restorations • a minimum baseline shade of A3 on 1 or more of the upper front teeth Exclusion criteria: • orthodontics bands, partial removable dentures • advanced periodontal disease, tumours of the soft or hard tissues • 5 or more carious lesions requiring immediate restorative treatment • allergy history, participation in another clinical study within 1 month prior to the study, recent whitening or bleaching of teeth • pregnant women • medical conditions which would compromise the subject's safety Number randomised: 50 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 49. 1 dropout from control group
Interventions	Total number of intervention groups: 2 Experimental: tray-based 6% hydrogen peroxide Control: no treatment

Mohan 2008 *(Continued)*

	Duration of treatment: 14 days
Outcomes	Change in tooth shade Oral irritation Vita shade guide arranged based on lightness (B1 lightest and C4 darkest). 1 is lightest - 16 is darkest b*: decreased b* indicates reduced yellowness; ΔL: increased ΔL is increased brightness
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Significant tooth whitening was evident after 3 days treatment with the tray-based whitening system and colour improved with continued usage over 14 days. It also supports our previous study results that the WIO index is appropriate for assessing changes in tooth whiteness" Contact: Dr Naveen Mohan, Dental Health Unit, 3A Skelton House, Lloyd Street North, Manchester Science Park, Manchester, England M15 6SH, UK; iain.pretty@manchester.ac.uk (IA Pretty)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Balancing the 2 groups on the basis of baseline tooth colour, subjects were randomly assigned to either a tray-based bleaching system or a non-treatment control group." However, the method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Quote: "A parallel, examiner-blinded, stratified 2-group clinical study." No other details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "A parallel, examiner-blinded, stratified 2-group clinical study." No other details provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "A parallel, examiner-blinded, stratified 2-group clinical study." No other details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 dropout due to ill health was withdrawn from the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described are reported. The conclusion is in accordance with results
Other bias	Low risk	None

Mokhlis 2000

Methods	Title: clinical evaluation of carbamide peroxide and hydrogen peroxide whitening agents during day-time Trial design: split-mouth, double-blinded, randomised controlled trial Location: University Purdue, Indianapolis, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: funded by Ultradent products Inc.
Participants	Participants: not reported Total number: 24 Inclusion criteria: • 6 maxillary anterior teeth present and free of any restorative material covering more than 1/6 of their labial surfaces • 6 anterior teeth darker than B54 and lighter than B85 on the Trubyte Bioform Colour Ordered Shade Guide (Dentsply Trubyte) • at least 18 years of age • willing to sign a consent form and able to return for periodic examinations • willing to refrain from use of tobacco products during the study period Exclusion criteria: • medical condition that might interfere with the study results or require special attention • Gingival Index score > 1 or gross pathology in the mouth • tetracycline-stained teeth or having undergone endodontic therapy in any of the maxillary anterior teeth • use of professionally-applied tooth whiteners within the past 5 years • use of any kind of tobacco products during the past 30 days • pregnant or lactating women Number randomised: 24 Method of randomisation: reported Method of allocation concealment: reported Method of blinding: not reported Number evaluated: 24
Interventions	Total number of intervention groups: 2 20% carbamide peroxide gel 7.5% hydrogen peroxide gel Duration of treatment: 2 weeks
Outcomes	Change in colour: ΔL, a*, b* values were recorded. Increase in L and reduction in b* indicated whitening Tooth and soft tissue sensitivity: 5-point scale: 1 none; 2 mild; 3 moderate; 4 considerable; and 5 severe
Notes	Sample size calculation: no

Mokhlis 2000 *(Continued)*

	Adverse effects: tooth and soft tissue sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Use of the 20% CP resulted in significantly more lightness than the 7.5% HP during the first 14 days of the study, but at the end of the study, there was no significant difference between products with regard to tooth lightness. In addition, the authors found no statistically significant difference between products with regard to gingival or tooth sensitivity" Contact: GR Mokhlis, Indiana University School of Dentistry, Indianapolis, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The subjects were randomised according to the baseline shade guide into 2 groups by a study monitor not directly involved in the study"
Allocation concealment (selection bias)	Low risk	Quote: "A study monitor assigned side of the mouth and the other gel to the opposite side. The monitor then labelled each box of bleaching gel accordingly"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blinded study but method of blinding not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blinded study but method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 24 patients completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Myers 2003

Methods	Title: clinical evaluation of a 3% hydrogen peroxide tooth whitening gel Trial design: double-blinded, placebo-controlled, randomised trial Location: School of Dentistry, Medical College of Georgia, Augusta, Georgia, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Applied Dental Sciences
Participants	Participants: age not reported Total number: 65

Myers 2003 *(Continued)*

	Inclusion criteria: • 21 years of age and above • A3 or darker on vita shade guide Exclusion criteria: • persons with significant medical problems or needing antibiotic premedication • pregnant or nursing women • persons with active dental caries or periodontal disease • persons with a history of vital bleaching • tetracycline staining Number randomised: 65 Method of randomisation: randomisation table by statistician Method of allocation concealment: syringes were labelled with the participant number. A single labelled syringe of gel was retained from each participant's box for later testing if needed Method of blinding: not reported Number evaluated: 65
Interventions	Total number of intervention groups: 2 3% hydrogen peroxide Nightguard gel Placebo Duration of treatment: 2 weeks
Outcomes	Colour change: Vita shade guide arranged base on lightness: 1 lightest (C1) to 16 darkest (B4) Dental sensitivity Irritation to tongue, gingiva, and throat
Notes	Sample size calculation: not reported Adverse effects: sensitivity in tongue and gingiva, dental sensitivity to hot and cold Health-related quality of life: not reported Key conclusions of the study authors: "Patient-applied NGVB with a 3% hydrogen peroxide gel for 30 minutes 3 times a day for 2 weeks was effective in whitening teeth an average of 4.2 Vita shade tabs. The lightening effect was maintained at 6 months, and the side effects with this agent were similar to other whitening agents. The use of this material could be considered for patients who cannot comply with the regimen" Contact: Michael L Myers, Department of Oral Rehabilitation, School of Dentistry, Medical College of Georgia, Augusta, Georgia 3091 USA; mmyers@mail.mcg.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomisation table was prepared by the lead statistician (CMR), who also maintained participant identification numbers used throughout the study"

Myers 2003 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "A randomisation table was prepared by the lead statistician (CMR), who also maintained participant identification numbers used throughout the study..... The outside of the box and the individual syringes were labelled with the paticipant number"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blinded study but method of blinding not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blinded study but method of blinding not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts reported
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Nathoo 1994

Methods	Title: clinical evaluation of Colgate Platinum professional tooth whitening system and Rembrandt lightening bleaching gel Trial design: single-blinded, randomised, parallel-group clinical trial Location: Colgate Palmolive Research Centre, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: not reported Total number: 40 Inclusion criteria: not mentioned Exclusion criteria: not mentioned Number randomised: 40 (n = 20 per group) Method of randomisation: not reported Method of allocation concealment: reported Method of blinding: not reported Number evaluated: 38 (1 dropout from each group: n = 19 in each group)
Interventions	Total number of intervention groups: 2 (tray versus tray)

Nathoo 1994 *(Continued)*

	10% urea peroxide, 30 minutes twice daily (Colgate Platinum) 10% urea peroxide, 30 minutes twice daily (Rembrandt lightening) Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade (objective assessment): increase in L and reduction in b* indicates whitening Improvement in tooth shade (subjective assessment): Vita shade guide arrange in order of lightness: percentage increase
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Colgate Platinum was 46% more effective at tooth whitening after 1 week, and 96% more effective after 2 weeks of treatment. The results demonstrated that the Colgate product was significantly superior versus Rembrandt at increasing tooth whiteness (increase in delta E), and tooth lightness (increase in delta L*). No adverse reactions were noted on clinical examination" Correspondence required: no Contact: Saleem A Nathoo, Colgate Palmolive Research Centre, Piscataway, New Jersey, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Single-blinded, randomised, parallel-group clinical trial." However, method of randomisation not reported
Allocation concealment (selection bias)	Low risk	Quote: "The identity of the products was concealed neither the subjects nor investigator were informed about the identity of products or to which group the individual belonged"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The identity of the products was concealed neither the subjects nor investigator were informed about the identity of products nor to which group the individual belonged" but details of the blinding method are not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Single-blinded, randomised, parallel-group clinical trial." However, method is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Of the 40 participants 38 participants completed the study (1 dropout from each group)" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Nathoo 2001

Methods	Title: comparative 7-day clinical evaluation of 2 tooth whitening products Trial design: double-blinded, parallel-group, randomised controlled clinical trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 65 years old Total number: 60 Inclusion criteria: adults with shade darker than A3 Exclusion criteria: not reported Number randomised: 60 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: syringes were coded and wrapped Number evaluated: 58
Interventions	Total number of intervention groups: 2 5% carbamide peroxide in tray 10% carbamide peroxide in tray Duration of treatment: 1 week, 6 to 8 hours per day
Outcomes	Improvement in tooth shade: Vita shade guide: tabs arranged from dark to light ΔL, a*, b* values: increase in ΔL and decrease in b* indicates lightening of teeth
Notes	Sample size calculation: not reported Adverse effects: hypersensitivity: sensitivity as reported - as yes or no questions Health-related quality of life: not reported Key conclusions of the study authors: "...whitening data showed that there was no significant difference between the 2 products after 1 week. The data suggest that these products are clinically equivalent for tooth whitening. However, the subjective data collected on tooth hypersensitivity showed that the product containing 5% carbamide peroxide was associated with less discomfort. Of the group using the 5% carbamide peroxide product, 20% reported transient sensitivity of their teeth after product use for 1 week compared with 53% of the group using the product with 10% carbamide peroxide. The product containing 5% carbamide peroxide was associated with less tooth hypersensitivity after 1 week of application" Correspondence required: no Contact: Saleem A Nathoo, Colgate Palmolive Research Centre, Piscataway, New Jersey, USA

Nathoo 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Double-blinded, randomised, controlled, parallel-group clinica trial." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The identity of the products were wrapped, neither the investigator no subjects were informed about.."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The identity of the products were wrapped, neither the investigator no subjects were informed about.."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "of the 60 participants who began the study 29 matched pairs (n = 58) remained throughout the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Nathoo 2002

Methods	Title: efficacy of novel, non-tray paint on 18% carbamide peroxide gel Trial design: double-blinded, parallel-group, randomised trial Location: Colgate Palmolive Research Centre, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 58 years old. Mean age 39.79 years Total number: 80 Inclusion criteria: • A3 shade or darker Exclusion criteria: • orthodontic treatment • restoration or crowns

Nathoo 2002 *(Continued)*

	Number randomised: not reported Method of randomisation: method not reported Method of allocation concealment: method not reported Method of blinding: non-removable white packing with patient identification number Number evaluated: 77
Interventions	Total number of intervention groups: 2 18% carbamide peroxide paint-on gel Placebo Duration of treatment: 21 days
Outcomes	Change in tooth shade Vita shade guide arranged base on lightness: 1 lightest (C1) to 16 darkest (B4)
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Study showed that subjects' teeth in the liquid whitening gel-treated group exhibited an overall improvement and a 3.5-shade difference compared with teeth in the placebo gel group. No soft tissue adverse reaction were reported" Contact: Saleem A Nathoo, Colgate Palmolive Research Centre, Piscataway, New Jersey, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Qualifying subjects were then stratified... and randomly assigned within strata to one of the study treatment groups.." However, the method by which randomisation was done is not mentioned in the article
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "For blinding, all products were overwrapped with a non-removable white label containing a unique subject identification number"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number of patients randomised were 80. However, there were 3 dropouts. Quote: "Subjects who did not complete the study dropped out for reasons unrelated to the use of the treatments or adverse events" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size

Nathoo 2002 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes mentioned are reported adequately. Conclusion conforms to results
Other bias	Low risk	None

Nathoo 2003

Methods	Title: comparative clinical investigation of tooth whitening efficacy of 2 whitening gels Trial design: randomised, double-blinded, parallel-group trial Location: Oral Health Clinical Services, Piscataway, New Jersey, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Colgate Palmolive
Participants	Participants: 18 to 70 years old. Mean age 28.5 years Total number: 59 Inclusion criteria: • 18 to 70 years of age • all maxillary anterior present with no restoration • no allergy to any of the ingredients of bleaching agent • Vita shade of A3 or darker Exclusion criteria: • undergoing orthodontic treatment • anterior tooth with prosthesis or veneers, crowns • tumour of hard or soft tissues • pregnant/lactating females • oral prophylaxis in month or use of any whitening products • any illness Number randomised: 59 Method of randomisation: not mentioned Method of allocation concealment: not mentioned Method of blinding: not mentioned Number evaluated: 59
Interventions	Total number of intervention groups: 2 Gel I: 25% carbamide peroxide Gel II: 8.7% hydrogen peroxide Duration of treatment: 3 weeks
Outcomes	Improvement in tooth shade

Nathoo 2003 *(Continued)*

	The shade guide was arranged with 16-shade tabs in order from B1 (1) to C4 (16)
Notes	Sample size calculation: not reported Adverse effects: none reported Health-related quality of life: not reported Key conclusions of the study authors: "The authors concluded that all subjects exhibited statically significant tooth shade lightening. There was no significant difference in the between both gels for one time night usage for 2/3 weeks application. No adverse reaction was noted" Correspondence required: no Contact: Dr William DeVizio, William_devizio@colpal.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All the participants completed the study"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Navarra 2014

Methods	Title: effects of 2 10% carbamide peroxide Nightguard bleaching agents, with and without desensitizer, on enamel and sensitivity: an in vivo study Trial design: blinded, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported

Navarra 2014 *(Continued)*

	Funding source: supported, in part, by grants from MIUR (Italy)
Participants	Participants: 20 to 50 years old. Mean age 25.3 years Total number: 80 Inclusion criteria: not reported Exclusion criteria: • smoking, pregnancy or breastfeeding • history of previous bleaching treatment • dentine hypersensitivity caused by caries lesions • fracture of restorations, chipped teeth, marginal gaps, post-operative sensitivity • teeth with cervical fillings, and recent use of desensitizing toothpaste Number randomised: 20 Method of randomisation: not reported Method of allocation concealment: reported Method of blinding: not reported Number evaluated: 20
Interventions	Total number of intervention groups: 2 10% carbamide peroxide with fluoride and potassium nitrate in tray 10% carbamide peroxide without desensitizing agents in tray Duration of treatment: 2 weeks
Outcomes	Improvement in tooth colour ΔL, a*, b*, ΔW values were recorded. Increase in ΔL and reduction in b* indicated whitening
Notes	Sample size calculation: not reported Adverse effects: sensitivity Key conclusions of the study authors: "The use of 10% carbamide peroxide gel with fluoride and potassium nitrate reduced the incidence of sensitivity during the bleaching treatment compared to a bleaching agent that did not contain desensitizing agents. The bleaching effectiveness of the tested products was comparable" Correspondence required: no Contact: M Cadenaro, m.cadenaro@fmc.units.it

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "An operator not involved in the research protocol performed the randomisation." However, method of randomisation is not reported
Allocation concealment (selection bias)	Low risk	Quote: "allocated groups were recorded on cards contained in sequentially numbered, sealed envelopes that were blindly assigned"

Navarra 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "blinded randomised controlled trial." However, method of blinding is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "blinded randomised controlled trial." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Oliveira 2013

Methods	Title: safety and efficacy of a high-adhesion whitening strip under extended wear regimen Trial design: randomised, blinded, parallel-group trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 19 to 64 years old. Mean age 42 years Total number: 29 Inclusion criteria: • 18 to 65 years of age • agree not to participate in any other oral/dental product studies during the course of this study • delay of any elective dentistry (including dental prophylaxis) until the study had been completed • refrain from the use of any non-study oral care products once assigned to treatment • return for all scheduled visits and follow study procedures • at least 4 gradable maxillary anterior teeth with a Vita shade score of A2 or darker Exclusion criteria: • teeth previously bleached using a professional bleaching treatment, over-the-counter bleaching kit, or investigational bleaching product • undergoing treatment for gingivitis, periodontitis, or caries • self-reported tooth sensitivity • fixed orthodontic appliances on the facial surfaces of the maxillary arch • dental crowns or large composite restorations on the facial surfaces of gradable maxillary anterior teeth • oral pathosis requiring prompt treatment or gross neglect of oral home care, and/or other signs indicating that the integrity of the data collected for that subject was compromised

Oliveira 2013 *(Continued)*

	• teeth that could not be imaged • meaningful malocclusion that would impact on treatment or imaging • teeth with severe or atypical intrinsic staining, such as that caused by tetracycline, fluorosis or hypocalcification Number randomised: 29 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: blinded test kits Number evaluated: 28
Interventions	Total number of intervention groups: 2 9.5% hydrogen peroxide gel strips 10% hydrogen peroxide gel strips Duration of treatment: 9 days
Outcomes	Improvement in tooth shade. ΔL, a*, b* values: increase in ΔL and decrease in b* indicates lightening of teeth
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "The 2-hour regimen for the 9.5% hydrogen peroxide high-adhesion whitening strip was more efficient for tooth whitening than the 30-minute regimen of 10% hydrogen peroxide whitening strip. Both treatments were well tolerated and the use of the test products during the study time frame was considered safe" Contact: GM Oliveira, gmoliv03@louisville.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "..subjects were randomly assigned to 1 of the 2 groups.... properly balanced for age and baseline tooth colour." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "A randomised, blinded, parallel group, single centre..... All test products and related instructions for use were packaged in blinded test kits with appropriate research labeling for distribution." No other details given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "A randomised, blinded, parallel group, single centre..... oral examination was conducted by an examiner blinded to treatment assignment to identify possible changes in oral status..." No other details given
Incomplete outcome data (attrition bias)	Low risk	Quote: "1 subject in the 2-hour strip group missed the day 5 visit"

Oliveira 2013 *(Continued)*

All outcomes		Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Papas 2009

Methods	Title: placebo-controlled clinical trial of use of 10% hydrogen peroxide whitening strips for medication-induced xerostomia Trial design: randomised, double-blinded, placebo-controlled clinical trial Location: University School of Dental Medicine and New England Medical Center, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: supported, in part, by Procter & Gamble
Participants	Participants: mean age 50 years Total number: 42 Inclusion criteria: • 4 or more anterior teeth • xerogenic medication history and symptoms, subjects had to present with an unstimulated salivary flow ^ 0.2 ml/min • Vita shade score of A2 or darker • adults 18 and above Exclusion criteria: • previous vital bleaching, apparent caries, periodontal disease • chlorhexidine mouthwas used • history of dentine hypersensitivity Number randomised: 42 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: identical package and coded Number evaluated: 40 (1 withdrew and 1 did not report after 15 days)
Interventions	Total number of intervention groups: 2 Control: placebo Experimental: 10% hydrogen peroxide whitening strips Duration of treatment: 2 weeks

Papas 2009 *(Continued)*

Outcomes	Tooth colour change Oral irritation and sensitivity b*: decreased b* indicates reduced yellowness; ΔL: increased ΔL is increased brightness
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and gingival irritation Key conclusions of the study authors: "At day 8, the peroxide group experienced colour improvement relative to baseline and placebo. Mild and transient tooth sensitivity represented the most common adverse events. No subject discontinued treatment due to a product-related adverse event" Contact: Athena S Papas, Tufts School of Dental Medicine, 1 Kneeland Street, Boston, MA 02111, USA; athena.papas@tufts.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A randomised double-blinded placebo-controlled clinical trial was conducted... eligible subjects were randomly assigned to .." However, the method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Except for the presence or absence of peroxide, the test strips were identical in appearance. The test strips (peroxide or placebo) were dispensed in a small, white, cardboard box with instructions specifying twice daily strip application for 30 minutes before toothbrushing. To further ensure blinding, each box was labelled only with a unique subject identification number and necessary contact information"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 subject from placebo group voluntarily withdrew from the study.." Comment: 1 participant withdrew and 1 did not report after 15 days. Plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes mentioned are reported adequately. Conclusions are in accordance with the results
Other bias	Low risk	None

Porciani 2006

Methods	Title: whitening effect by stain inhibition from a chewing gum with sodium hexametaphosphate in a controlled 12-week single-blinded trial Trial design: randomised, single-blinded, cross-over trial

Porciani 2006 *(Continued)*

	Location: University of Siena, Dental School, Siena, Italy Language: English Number of centres: 1 Recruitment period: not reported Funding source: Perfetti Van Melle
Participants	Participants: mean age 30.6 years Total number: 54 Inclusion criteria: • subjects had to present with 8 incisors without any fillings, crowns, or fixed orthodontic appliances Exclusion criteria: • exhibit no oral or facial pain or disease • more than 3 cups of tea and/or coffee Number randomised: 54 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 54
Interventions	Total number of intervention groups: 2 4% sodium hexametaphosphate Placebo Duration of treatment: 12 weeks
Outcomes	Reduction in stain (0 = no stain, 1 = light stain, 2 = moderate stain, 3 = heavy stain) Stain area (0 = no stain, 1 = stain covering up to 1/3 of the region, 2 = stain covering from 1/3 to 2/3 of the region, and 3 = stain covering greater than 2/3 of the region) Stain intensity Smoker versus non-smokers
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "The results indicated that chewing gum containing sodium hexametaphosphate reduced induced stain formation by 33% compared to no gum treatment" Correspondence required: no Contact: Francesco Porciani, piercateadsl@libero.it
Risk of bias	

Porciani 2006 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "were randomly assigned to the test gum or no-gum group.." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the teeth were scored for stain deposits by the same examiner who was blinded to the product assignments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 54 subjects (27 females and 27 males) initially enrolled in the study completed it"
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Porciani 2010

Methods	Title: effect on dental stain occurrence by chewing gum containing sodium tripolyphosphate Trial design: double-blinded, parallel-group, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Perfetti van Melle
Participants	Participants: 18 to 54 years old. Mean age 28.9 years Total number: 111 Inclusion criteria: • presence of all anterior teeth • no more than 3 restorations • no orthodontic treatment • Lobene stain index between 0.33 and 1.5 Exclusion criteria: • diabetes or systemic disease • oral and facial pain • sensitivity to polyphosphate-containing dentifrices

Porciani 2010 *(Continued)*

	Number randomised: 111 Method of randomisation: random table Method of allocation concealment: not reported Method of blinding: similar looking package, shape, flavour and weight of the chewing gum. Participants instructed not to discuss the treatment they were receiving Number evaluated: 108. 3 participants dropped out from experiment group
Interventions	Total number of intervention groups: 2 Experimental: sodium tripolyphosphate (1%) containing gum Control: placebo Duration of treatment: 6 weeks
Outcomes	Reduction in stain intensity and extent of stain Lobene modified index: smaller value shows improvement Stain composite index: smaller value shows improvement
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "This trial showed a reduction in dental stain by a chewing gum containing sodium tripolyphosphate after 6 weeks" Contact: PF Porciani, piercateadsl@libero.it

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Each subject entered in the test or control group using a random table .."
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Both chewing gums had the same flavour, weight, shape, colour, and packaging so that the participants were blinded as to the identity of the gum" Comment: additionally, participants were instructed not to tell other subjects to which group they were assigned in order to minimize inadvertent disclosure to the study participants and staff
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Data were scored by the same blinded operator for all measurements"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "... 3 eventually dropped out, though the cause was unrelated to polyphosphates"

Porciani 2010 *(Continued)*

		Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes mentioned were reported adequately. Conclusion reflected study results (in the abstract)
Other bias	Low risk	None

Russell 1996

Methods	Title: dentist-supervised home bleaching with 10% carbamide peroxide gel Trial design: double-blinded, randomised controlled trial Location: Medical College of Georgia, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 22 to 79 years. Mean age 43.9 years Total number: 50 Inclusion criteria: • healthy adults Exclusion criteria: • previous vital bleaching • apparent caries, periodontal disease • orthodontic appliances • anterior restorations • history of dentine hypersensitivity • pregnant or nursing woman • tetracycline stains • on antibiotic medication Number randomised: 50 Method of randomisation: randomisation table Method of allocation concealment: not reported Method of blinding: both gels were provided by the manufacturer in small kits containing syringes Number evaluated: 50
Interventions	Total number of intervention groups: 2 Experimental: carbamide peroxide 10% tray Control: placebo Duration of treatment: 2 weeks (follow-up of 6 months)

Russell 1996 *(Continued)*

Outcomes	Lightening of teeth Vita shade guide arrange in ascending order for lightness. Rank 1: darkest (B4), rank 16: lightness (C1)
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "The 10% carbamide peroxide product and treatment regimen for vital bleaching used in this study have been shown to produce a significant lightening effect immediately after treatment consistent with other studies. In addition, this study shows that the lightening effect lasts at least 6 months for the majority of subjects" Contact: Carl M Russell, Office of Biostatistics, Medical College of Georgia, Augusta, GA 30912-4900, USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation table containing subject identification numbers and group assignment was prepared by the lead statistician"
Allocation concealment (selection bias)	Unclear risk	Not done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The placebo treatment gel was the same as the active gel except the carbamide peroxide was omitted. Both gels were provided by the manufacturer in small kits containing syringes.."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts reported. The number randomised were the number assessed in both groups over the 6-month period
Selective reporting (reporting bias)	Low risk	All outcomes described are reported adequately. Conclusions are in accordance with the results
Other bias	Low risk	None

Shahidi 2005

Methods	Title: randomised controlled trial of 10% hydrogen peroxide whitening strips Trial design: randomised, double-blinded clinical trial Location: Hill Top Research Inc, USA Language: English Number of centres: 1 Recruitment period: not reported

Shahidi 2005 *(Continued)*

	Funding source: Procter & Gamble
Participants	Participants: 19 to 48 years old. Mean age 32.4 years Total number: 40 Inclusion criteria: not reported Exclusion criteria: • no previous tooth whitening • sensitivity or exclusive restoration Number randomised: 40 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: reported Number evaluated: 35
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide 0.2 mm strip 10% hydrogen peroxide 0.13 mm strip Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade. ΔL, a*, b* values: increase in ΔL and decrease in b* indicates lightening of teeth
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Key conclusions of the study authors: "Vital bleaching with 10% hydrogen peroxide strips at 1 week was as effective as 6% hydrogen peroxide strips used for 2 weeks. At the end of 2 weeks 10% hydrogen peroxide was better than 6% hydrogen peroxide. Both treatments were generally well tolerated, with mild and transient tooth sensitivity or oral irritation representing the most common adverse events" Contact: Robert Geralch, geralchgw@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomised, double-blinded clinical trial.... Subjects were randomly assigned to 1 of the strip groups." However, the method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The test and experimental strips were identical in size... each strip was packaged in an individual white foil pouch, with subject identification number"

Shahidi 2005 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	5 dropouts at the end of the trial. Reason for dropouts not mentioned. We are not sure if the plausible effect size (difference in means) among missing outcomes may have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcome described are reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Swift 2004

Methods	Title: 3-week clinical trial of a 14% hydrogen peroxide, strip-based bleaching system Trial design: blinded, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 19 to 70 years old. Mean age 50 years Total number: 29 Inclusion criteria: • healthy subjects with A2 or darker shade Exclusion criteria: • any pre-existing oral or medical condition • crowns or large facial composite restorations on the maxillary anterior teeth • teeth previously • current treatment for gingivitis, periodontitis, or caries • currently using a chlorhexidine or Listerine mouthrinse • teeth with severe or atypical intrinsic staining • meaningful malalignment • fixed orthodontic appliances Number randomised: 29 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 28
Interventions	Total number of intervention groups: 2

Swift 2004 *(Continued)*

	14% hydrogen peroxide bleaching strips Placebo Duration of treatment: 3 weeks
Outcomes	Change in tooth colour Vita shade guide arranged base on lightness: 1 lightest (C1) to 16 darkest (B4) Plaque and Gingival Index
Notes	Sample size calculation: not reported Adverse effects: gingival irritation and tooth sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Professional hydrogen peroxide strips evaluated in this clinical trial proved effective for tooth whitening with minimal side effects. Only 2 of the 13 subjects in the experimental group reported any tooth sensitivity, and only 3 reported any soft tissue irritation. The symptoms were described as mild in each case. In addition, changes in the gingival index and plaque index were very minor" Contact: Edward Swift, ed_swift@dentistry.unc.edu

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants were stratified and randomised to treatment groups based on their VITA shade and age." However, the method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "29 subjects were enrolled in the study and received either the experimental or placebo product; 28 completed the clinical trial" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described are reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Swift 2009

Methods	Title: effects of duration of whitening strip treatment on tooth colour Trial design: randomised, double-blinded, placebo-controlled clinical trial Location: University of North Carolina, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble (authors are employed by this company)
Participants	Participants: 25 to 58 years Total number: 40 Inclusion criteria: • A3 or darker shades • healthy individuals Exclusion criteria: • current tooth sensitivity • orthodontic treatment • aesthetic restorations Number randomised: 40 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: blinded test kits with similar over packing Number evaluated: week 2 n = 39, week 4 n = 36, week 6 n = 37 (week 2: 1 dropout from peroxide group; week 4: 1 dropout from peroxide and 3 from placebo; and week 6: 1 dropout from peroxide and 2 dropouts from placebo group)
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide gel strips Placebo Duration of treatment: 2 weeks
Outcomes	Change in tooth shade b*: decreased b* indicates reduced yellowness; ΔL: increased ΔL is increased brightness
Notes	Sample size calculation: not reported Adverse effects: tooth sensitivity and oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "Twice-daily use of 6% hydrogen peroxide whitening strips resulted in teeth becoming lighter and less yellow versus baseline and placebo during initial 2-week use, with no evidence of placebo response during sustained (weeks 2-6) use" Contact: Edward Swift, ed_swift@dentistry.unc.edu

Swift 2009 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A randomised double-blinded placebo-controlled clinical trial was conducted... After balancing for starting tooth colour and age, subjects were randomly assigned to peroxide or placebo strips." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo strips were identical to the test strips. Quote: "All test products and instructions for use were packaged in a blinded test kit.."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 subject in peroxide group was dismissed early as a recall failure. 4 other subjects completed the study but were excluded from the statistical analysis because of missed visits or non-compliance" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes discussed have been reported adequately. Conclusions are in accordance with the results
Other bias	Low risk	Outliers in the data sets are removed. It may have an effect on the results

Tam 2001

Methods	Title: effect of potassium nitrate and fluoride on carbamide peroxide bleaching Trial design: split-mouth, double-blinded, randomised clinical trial Location: University of Toronto, Canada Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: 20 to 53 years old with a mean age of 31 (10) years Total number: 42 Inclusion criteria: not reported Exclusion criteria: no previous history of desensitizing agents Number randomised: not reported

Tam 2001 *(Continued)*

	Method of randomisation: not reported Method of allocation concealment: syringes were randomly numbered and selected for use Method of blinding: identical packs Number evaluated: 40
Interventions	Total number of intervention groups: 2 10% carbamide peroxide with 3% potassium nitrate and 0.11 fluoride ion wt/vol 10% carbamide peroxide Duration of treatment: 2 weeks
Outcomes	Tooth sensitivity Tooth whitening: patient-reported improvement
Notes	Sample size calculation: not reported Adverse effects: sensitivity Key conclusions of the study authors: "A 10% carbamide peroxide bleaching gel containing potassium nitrate and fluoride produced less tooth sensitivity than did the control bleaching gel during a 2-week at-home bleaching treatment" Correspondence required: no Contact: Dr Laura Tam, laura.tam@utotonto.ca

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "double-blinded randomised clinical trial." However, method of randomisation is not reported
Allocation concealment (selection bias)	Unclear risk	Quote: "syringes were randomly numbered and selected for use on either the left or right side of each patient's dental arch" Comment: we are not sure if the person allocating the participants and the person conducting the study are the same
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "formulations were manufactured specifically for this study (Ultradent) and were packaged identically for..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded randomised clinical trial." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "1 patient chose to discontinue treatment .... A total of 9 treatment days (out of a potential total of 294 treatment days) were missed by the patients, either because of general tooth sensitivity or for personal reasons" Comment: no clear mention of dropouts in the article

Tam 2001 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes discussed have been reported adequately. Conclusions are in accordance with the results
Other bias	Low risk	None

Tsubura 2005

Methods	Title: clinical evaluation of a new bleaching product Polanight in a Japanese population Trial design: split-mouth, randomised controlled trial Location: private dental clinic Language: English Number of centres: 1 Recruitment period: not reported Funding source: SDI Ltd
Participants	Participants: 18 to 47 years old. Mean age 30 years Total number: 58 Inclusion criteria: not reported Exclusion criteria: not reported Number randomised: 58 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 58
Interventions	Total number of intervention groups: 2 Polanight: 10% carbamide peroxide Opalescence: 10% carbamide peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth colour ΔL, a*, b* values: increase in ΔL and decrease in b* indicates lightening of teeth
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Treatment with either agent demonstrated significant bleaching effects produced by the treatment. Bleaching with PN was considered more effective than that with OP in the young patient group and in the women" Correspondence required: no

Tsubura 2005 *(Continued)*

Contact: R Yamaguchi, hshimo@ngt.ndu.ac.jp

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...were randomly selected from the patients visiting." However, method of randomisation is not described
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Turkun 2010

Methods	Title: 1-year clinical evaluation of the efficacy of a new daytime at-home bleaching technique Trial design: parallel group randomised controlled clinical trial Location: Ege University, Turkey Language: English Number of centres: 1 Recruitment period: not reported Funding source: no
Participants	Participants: 20 to 30 years old Total number: 20 Inclusion criteria: • have all maxillary and mandibular anterior teeth with a shade mean of C1 or darker • no caries and restoration on the teeth to be bleached • be between 20 and 30 years old • be able to return for periodic controls • consuming the products that stain teeth (coffee, red wine, tea, etc.) not more than 5 times in a day

Turkun 2010 *(Continued)*

	Exclusion criteria: • poor general or dental health • fixed orthodontic appliances • having hypersensitive teeth • smoking • current or previous use of bleaching agents • pregnant or lactating women • tetracycline-stained teeth • a history of allergies to tooth whitening products Number randomised: 20 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 20
Interventions	Total number of intervention groups: 2 28% carbamide peroxide gel in daytime non-custom-fit tray (Meta Tray) 10% carbamide peroxide gel in overnight custom-fit tray (Opalescence PF) Duration of treatment: 10 days
Outcomes	Improvement in tooth shade: ΔL, a*, b* values: increase in ΔL and decrease in b* indicates improvement Sensitivity: 0 - no changes noted, 1 - mild sensitivity, 2 - moderate sensitivity, and 3 - severe sensitivity
Notes	Sample size calculation: not mentioned Adverse effects: sensitivity Health-related quality of life: not mentioned Key conclusions of the study authors: "...daytime at-home bleaching system tested (Meta Tray) produced significant bleaching effects. However, the clinical efficacy of the overnight bleaching system was found superior to this new daytime at-home bleaching system. Al though the new bleaching system exhibited less tooth sensitivity probably because of the reduced contact time of the bleaching gel with tooth surfaces, the application of the bleaching agent with a non-customized tray provoked more gingival sensitivity in this group. The whitening effect remained similar 1 year after the bleaching"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "20 adult subjects .....were selected to participate in this randomised, controlled clinical trial." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	1 group had a custom-made tray while the other used a prefabricated tray. There is a high risk that participants get to know the difference

Turkun 2010 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...by an examiner who did not know the treatment details of the patients"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 20 participants completed this study"
Selective reporting (reporting bias)	Low risk	All outcomes described have been reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Walters 2004

Methods	Title: benefits of sodium hexametaphosphate-containing chewing gum for extrinsic stain inhibition Trial design: placebo-controlled, randomised, examiner-blinded, 2-period cross-over trial Location: London, UK Language: English Number of centres: 1 Recruitment period: not reported Funding source: author is employed by Procter & Gamble
Participants	Participants: 22 to 58 years old. Mean age 30.4 years Total number: 11 Inclusion criteria: • 18 years old • minimum of 16 natural teeth, including at least 7 of the 8 anterior incisor teeth Exclusion criteria: • known hypersensitivity to chlorhexidine digluconate or polyphosphates • anterior facial restorations • evidence of temporomandibular joint dysfunction • presence of oral ulcers, self-reported diabetes • self-reported pregnancy Number randomised: 11 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 10. 1 dropout from the experimental (chewing gum first/negative control gum second) due to an adverse event
Interventions	Total number of intervention groups: 2 Experimental: 5.6% sodium hexametaphosphate chewing gum

Walters 2004 *(Continued)*

	Control: non-sodium hexametaphosphate chewing gum Duration of treatment: 3 days, 10 days washout period before cross-over
Outcomes	Reduction in induced extrinsic stains
Notes	Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Sodium hexametaphosphate-containing chewing gum can significantly reduce induced extrinsic dental stain formation, compared to a non-sodium hexametaphosphate chewing gum" Contact: Patricia A Walters, walters.pa@pg.com

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The study was a negative-controlled, examiner-blinded, randomised, 2-period cross-over design." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The study was a negative-controlled, examiner-blinded, randomised, 2-period cross-over design." However, method of blinding is not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The study was a negative-controlled, examiner-blinded, randomised, 2-period cross-over design." However, method of blinding is not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "1 subject in the experimental sequence dropped from the study due to an adverse event, reported and diagnosed by the examiner" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes mentioned are reported adequately. Conclusions are in accordance with results
Other bias	Low risk	None

Wong 2004

Methods	Title: randomised controlled trial of home tooth whitening products Trial design: randomised, double-blinded, single-centre clinical trial with 3 parallel groups Location: Hong Kong University Language: English Number of centres: 1

Wong 2004 *(Continued)*

	Recruitment period: not reported Funding source: none
Participants	Participants: 18 to 30 years old Total number: 157 Inclusion criteria: • 18 to 30 years of age and in good general health • wanted to have their teeth whitened • had at least 3 anterior maxillary teeth with tooth shade of Vita A2 Exclusion criteria: • had teeth previously bleached • had dental restorations in the maxillary anterior teeth • had dental work planned or were currently having dental treatment • had clinical evidence of periodontitis, dental caries, severe malocclusion or severe staining (e.g. tetracycline stains) Number randomised: 87 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: brands covered with foil Number evaluated: 63
Interventions	Total number of intervention groups: 3 6% hydrogen peroxide strip. Twice daily for 2 weeks 18% carbamide peroxide paint-on gel Placebo: non-whitening toothpaste Duration of treatment: 2 weeks
Outcomes	Improvement in tooth whitening: ΔL, a*, b*: increase in ΔL and reduction in b* indicates whitening Satisfaction of tooth whitening: 9-point Likert scale
Notes	Sample size calculation: none Adverse effects: irritation of gums or teeth Health-related quality of life: 0 to 4 (never - hardly ever - occasionally - fairly often - often), Oral Health Impact Profile Key conclusions of the study authors: "Crest Whitestrips (6.5% hydrogen peroxide) and Colgate Simply White (18% carbamide peroxide) are both effective in tooth whitening with the former being more effective" Correspondence required: no Contact: not reported
Risk of bias	

Wong 2004 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subject inclusion and exclusion criteria, and randomly allocated into 1 of the following 3 groups." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "brands of all study products were masked by covering the products with adhesive aluminium foils"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "randomised controlled, double-blinded, single-center clinical trial." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Each study group started with 29 subjects and the 3 groups W, S, and P ended with 22, 21 and 20 subjects respectively" Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Xu 2007

Methods	Title: randomised clinical trial comparing whitening strips, paint-on gel and negative control Trial design: randomised, examiner-blinded, placebo-controlled study Location: Shanghai Second Medical University, Shanghai, China Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble
Participants	Participants: 18 to 45 years old. Mean age 21.85 years. 92% females. Total number: 52 Inclusion criteria: not reported Exclusion criteria: not reported Number randomised: 52 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: similar kits

Xu 2007 *(Continued)*

	Number evaluated: 49
Interventions	Total number of intervention groups: 3 Whitening strips 6% hydrogen peroxide (n = 18), Paint-on gel 5.8% hydrogen peroxide (n = 17; 2 dropouts) Negative control (water rinse) (n = 17; 1 dropout) Duration of treatment: 8 days for whitening strip, 15 days for gel and water rinse
Outcomes	Change in tooth colour ΔL, a*, b* values were recorded. Increase in ΔL and reduction in b* indicates whitening of tooth
Notes	Sample size calculation: not reported Adverse effects: mild sensitivity in strip group Health-related quality of life: not reported Key conclusions of the study authors: "Despite similarities in starting concentration (6% hydrogen peroxide), the strip and paint-on gel differed significantly on improvement in yellowness, brightness, and redness, as well as overall colour improvement. These differences were achieved with one-half the treatment duration (7 versus 14 days) for strips compared to the paint-on gel. Since only 1 of the products used a barrier, differences in residence time of the peroxide gel under a strip versus the barrier-free paint-on gel may have contributed to the relative clinical response of these 2 peroxide-containing products" Contact: Dr Xu, xuxiao@smmail.cn

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "subjects were randomly assigned to peroxide whitening strips (the positive control), paint-on peroxide whitening gel, or water (the negative control)." However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Subjects were provided an identically appearing kit box labelled only with the unique subject number"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 18 subjects in the strip group completed the research, while 2 subjects in the paint-on group and 1 subject in the water rinse group failed to complete the study" Comment: plausible effect size (difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results

Xu 2007 *(Continued)*

Other bias	Low risk	None

Ziebolz 2007

Methods	Title: efficacy and oral side effects of 2 highly concentrated tray-based bleaching systems Trial design: randomised, 2-armed, parallel clinical study Location: University of Göttingen, Germany Number of centres: 1 Recruitment period: not reported Funding source: study supported by Kettenbach, Germany
Participants	Participants: 20 to 48 years old Total number: 60 Inclusion criteria: • restoration or caries free teeth • Vita shade score of A2 or darker • no crowns on upper cuspids or incisors Exclusion criteria: • tooth hypersensitivities • anterior restorations • poor oral hygiene • generalised gingival recession • caries, heavy structural alteration of the tooth structure • tetracycline or fluorosis staining Number randomised: 60 Method of randomisation: stratified, randomised distribution Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 56 (4 dropouts) - three dropouts in VW due to therapy pain and one dropout in OP due to therapy pain.
Interventions	Total number of intervention groups: 2 7.5% hydrogen peroxide gel in tray (Visalys) 20% carbamide peroxide gel in tray (Opalescence) Duration of treatment: 12 days
Outcomes	Tooth colour change: L*, a*, b* values: increase in L* and decrease in b* indicated lightening of teeth Hypersensitivity: 0 to 10 (0 = no hypersensitivity, 10 = high hypersensitivity) Acceptability: comfortable, slightly disturbing, uncomfortable or very uncomfortable

Ziebolz 2007 *(Continued)*

Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The bleaching systems demonstrated significant tooth colour improvement for Δb* and ΔL*. They did produce significantly different whitening response for Δb*, with Opalescence showing significant higher Δb*. After bleaching therapy, the intensity of tooth hypersensitivity was increased significantly compared to baseline, with no significant difference between both groups" Contact: Dr Dirk Ziebolz, dirk.ziebolz@zm-goettingen.de

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A stratified, randomised distribution of the subjects to the 2 treatment groups..." However, method is not reported
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "3 subjects from the Visalys group and 1 from the Opalescence group withdrew during bleaching therapy..." Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Ziebolz 2008

Methods	Title: influence of a desensitizing agent on efficacy of a paint-on bleaching agent Trial design: double-blinded, randomised controlled trial Location: University of Göttingen, Germany Language: English Number of centres: 1 Recruitment period: not reported

Ziebolz 2008 *(Continued)*

	Funding source: Ivoclar Vivadent, Schaan, Liechtenstein
Participants	Participants: mean age 26.27 years Total number: 80 Inclusion criteria: • caries and restoration free • Vita shade score of A2 or darker Exclusion criteria: • previous vital bleaching, apparent caries, periodontal disease • anterior restorations • pregnant and nursing women • tetracycline stains • xerostomia Number randomised: 80 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 67. 13 dropouts
Interventions	Total number of intervention groups: 2 Control: hydrogen peroxide 6% without desensitizers (n = 40, final 7 dropouts) Experimental: hydrogen peroxide 6% with desensitizer (n = 40, final 6 dropouts) Duration of treatment: 10 days
Outcomes	Tooth colour change: Vita shade guide Tooth hypersensitivity: 0 = no sensitivity, 10 = high sensitivity Acceptability: interview: comfortable, slightly disturbing, uncomfortable or very uncomfortable Tolerability: interview: comfortable, slightly disturbing, uncomfortable or very uncomfortable
Notes	Sample size calculation: not reported Adverse effects: sensitivity and irritation in both groups Key conclusions of the study authors: "treatment groups developed tooth hypersensitivities during bleaching therapy. The number of subjects exhibiting sensitivities after bleaching increased more in the group without application of VivaSens (plus 15.2%) than in the group with VivaSens (2.9%), but the difference between the groups was not significant. Lack of statistical significance might be due to the low increase of tooth sensitivities due to the bleaching. This relatively low incidence of tooth hypersensitivity might be explained by the low concentration of peroxide (6.0%) in the bleaching agent used in this study. It might be speculated that a distinct higher number of subjects with tooth hypersensitivities due the bleaching therapy in the control group (Group A) without VivaSens application might have better demonstrated the positive effect of the desensitizing agent" Contact: Dr Dirk Ziebolz, dirk.ziebolz@zm-goettingen.de
Risk of bias	

Ziebolz 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The 80 subjects were distributed randomly among 2 groups" However, method of randomisation is not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding is not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blinded, randomised, controlled, parallel-group clinical trial." However, method of blinding is not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "13 subjects failed to complete the 2-week study (1 from each group) for reasons unrelated to the study Comment: missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

CP = carbamide peroxide; HP = hydrogen peroxide; NGVB = nightguard vital bleaching; SE = standard error; STPP = sodium tripolyphosphate; VAS = visual analogue scale; WIO = whiteness index.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alkmin 2005	Study compared the effects of 2 bleaching agents on oral microbiota.
Amini 2009	Abstract: insufficient information to include.
Amini 2011	Abstract: insufficient information to include.
Anastasia 2010	Abstract: insufficient information to include.
Andreana 2000	Abstract: insufficient information to include.
Archila 2010	Abstract: insufficient information to include.
Auschill 2009	Abstract: insufficient information to include.
Browning 2001	Abstract: insufficient information to include.
Burgio 2001	Study involved in-office bleaching as intervention.
Cardoso 2010	Study compared the clinical effectiveness and tooth sensitivity associated with different bleaching agents in children.

Study	Reason for exclusion
Collins 2004	Study compared the effect of self-applied tooth whitening gel on oral soft tissue.
Corby 2014	Study compared the effect of hydrogen peroxide whitening strips in adolescent twins.
Curtis 1996	Study compared the effect of carbamide peroxide whitening gel on oral soft tissue.
de Geus 2015a	Controlled clinical trial evaluating the genotoxicity and efficacy of at-home bleaching in smokers and non-smokers.
de Geus 2015b	Controlled clinical trial evaluating tooth sensitivity in smokers.
Dickinson 2000	Abstract: insufficient information to include.
Donly 2001	Abstract: insufficient information to include.
Donly 2002	Study compared the use of whitening strips in children.
Donly 2002a	Study compared the use of whitening strips in children and adolescents.
Farrell 2006	The home-based bleach was applied professionally in the clinic.
Farrell 2008	Study compared the effect of hydrogen peroxide whitening strips on tooth sensitivity and oral irritation.
Fugaro 2004	Study evaluated the histological changes in dental pulp after nightguard vital bleaching.
Fugaro 2005	Study assessed the expression of specific neuropeptides associated with inflammation.
Garcia-Godoy 2012	Abstract: insufficient information to include.
Gerlach 2002c	The intervention included toothbrushing.
Gerlach 2002d	Abstract: insufficient information to include.
Gerlach 2002e	Study compared 2 professional tooth whitening systems for shade change using chroma meter.
Gerlach 2003a	One of the interventions included a whitening dentifrice.
Gerlach 2004a	One of the interventions included a whitening dentifrice.
Gerlach 2004c	Study evaluated the peroxide degradation and dilution kinetics of a bleaching agent.
Gerlach 2004d	Trial included teenagers and younger age group participants.
Godson 2001	Abstract: insufficient information to include.
Gursoy 2008	Study compared the effect of external tooth bleaching on dental plaque accumulation and discolouration.
Jadad 2011	Study evaluated the colour alterations with a new dental bleaching product in patients wearing orthodontic appliances.
Jorgensen 2002	Study compared the incidence of tooth sensitivity after home whitening treatment.
Karpinia 2003	One of the interventions included a whitening dentifrice.

Study	Reason for exclusion
Lee 2003	Abstract: insufficient information to include.
Leonard 2002	Study evaluated safety issues when using a 16% carbamide peroxide whitening solution.
Leonard 2004	Study evaluated the efficacy of a desensitizing agent used along with a bleaching agent.
Leonard 2007	Study evaluated effects on oral tissues and associated tooth sensitivity and patients' perceptions during tooth bleaching.
Lisante 2009	Abstract: insufficient information to include.
Loyola-Rodriguez 2003	Study included adolescents.
Majeed 2011	Abstract: insufficient information to include.
Marques 2012	Study compared salivary hydrogen peroxide release kinetics and potential toxicity of systemic exposure of 4 different whitening products.
Martin 2015	In-office bleaching was used in intervention.
Matis 1999	Study evaluated in vivo degradation rate of beaching gels in bleaching trays.
Matis 2002	Study compared different degradation of 15% carbamide peroxide.
Matis 2002a	A clinical evaluation of a bleaching agent used with and without reservoirs.
Matis 2005	Quasi-randomised controlled trial.
Mazur 2013	Abstract: insufficient information to include.
NCT02603354	Study involved in-office bleaching as intervention.
NCT02682329	Study involved in-office bleaching as intervention.
Perdigao 2013	Abstract: insufficient information to include.
Pinto 2014	Tooth whitening with hydrogen peroxide in adolescents.
Pinto 2017	Study compared whitening with hydrogen peroxide in adolescents.
Rezende 2013	Study compared the clinical effects of exposure to coffee during at-home vital bleaching.
Sagel 2001	Abstract: insufficient information to include.
Schiff 1994	Study is not about home-based bleaching.
Schulte 1993	Study evaluated clinical changes in the gingiva as a result of at-home bleaching.
Schulte 1994	Study evaluated and compared pulpal responses of teeth exposed to a bleaching agent.
Simon 2001	Trial comparing tooth whitening with peroxide-containing strips to a marketed whitening dentifrice.
Simon 2011	Abstract: insufficient information to include.

Study	Reason for exclusion
Smith 2001	Abstract: insufficient information to include.
Swift 2001	Abstract: insufficient information to include.
Tam 1999	Study participants included adolescents.
Walter 2011	Abstract: insufficient information to include.
Yankell 1997	Intervention used in the study (chewing gum) is excluded from this review.
Zantner 2006	In-office application was done for 1 group.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Barnes 1998

Methods	Title: clinical evaluation of a new 10% carbamide peroxide tooth-whitening agent Trial design: double-blinded clinical trial Location: University of Maryland Dental School, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dentsply
Participants	Participants: 18 to 65 years Total number: 61 Inclusion criteria: A3 or darker shade Exclusion criteria: not reported Number randomised: not reported Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: 50
Interventions	Total number of intervention groups: 2 groups 10% carbamide peroxide gel in tray Placebo Duration of treatment: 4 hours to overnight for 2 weeks
Outcomes	Improvement in tooth shade: 2 weeks, 3 months and 6 months Tooth sensitivity

Barnes 1998 *(Continued)*

	Gingival irritation
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The average shade change for the placebo users was less than 1 shade. The average shade change for the NUPRO Gold users was 6.96 shades. Tooth hypersensitivity varied from none to severe. Tissue irritation was minimal. The results of these evaluations indicate that NUPRO Gold is effective as a tooth whitening system, when administered properly under the supervision of a dentist, with commonly reported side effects of transient tooth sensitivity and minimal gingival sensitivity. Little or no change in tissue health was noted" Correspondence required: yes: unclear if it is a randomised controlled trial. Authors have been mailed requesting for the data Contact: Dr Douglas Barnes, University of Maryland, Maryland, USA

Bizhang 2017

Methods	Title: effectiveness of a new non-hydrogen peroxide bleaching agent after single use - a double-blind placebo-controlled short-term study Trial design: double-blinded randomised placebo-controlled trial Location: not reported in abstract Number of centres: 1 Recruitment period: not reported in abstract Funding source: not reported in abstract
Participants	Participants: not reported Total number: 40 Inclusion criteria: not reported in abstract Exclusion criteria: not reported in abstract Number randomised: 40 Method of randomisation: not reported in abstract Method of allocation concealment: not reported in abstract Method of blinding: not reported in abstract Number evaluated: not reported in abstract
Interventions	Total number of intervention groups: 2 Over-the-counter product Placebo Duration of treatment: 1 day
Outcomes	Improvement in tooth shade

Bizhang 2017 *(Continued)*

Notes	Yet to procure full text for this article

Braun 2007

Methods	Title: spectrophotometric and visual evaluation of vital tooth bleaching employing different carbamide peroxide concentrations Trial design: double-blinded randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Participants: not reported Total number: 30 Inclusion criteria: not reported Exclusion criteria: not reported Number randomised: 30 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: unmarked syringes Number evaluated: 30
Interventions	Total number of intervention groups: 3 0% carbamide peroxide 10% carbamide peroxide 17% carbamide peroxide Duration of treatment: 1 week
Outcomes	Improvement in tooth shade
Notes	Sample size calculation: not reported Adverse effects: not reported Key conclusions of the study authors: "The study indicates that higher concentration bleaching agents might whiten teeth faster with major changes in lightness and chroma. However, by bleaching daily for 1 week, similar effects can be achieved with both a high and a low concentration agent. After treatment, a regression of the resultant shade has to be expected" Correspondence required: yes: authors have been mailed requesting for missing data

Braun 2007 *(Continued)*

	Contact: Andreas Braun, andreas.braun@uni-bonn.de

Browning 2004

Methods	Title: safety and efficacy of a nightguard bleaching agent containing sodium fluoride and potassium nitrate Trial design: unknown
Participants	Participants: 22 Total number: 22 Number randomised: not clear Method of randomisation: not clear Method of allocation concealment: not clear Method of blinding: not clear Number evaluated: 22
Interventions	10% carbamide peroxide with potassium nitrate and sodium fluoride Placebo
Outcomes	Tooth whitening Sensitivity of teeth, gingiva, tongue and throat
Notes	Randomisation: not mentioned Sample size calculation: not reported Correspondence required: yes: authors have been mailed requesting for missing data Contact: Dr William Browning, wbrownin@mail.mcg.edu

Ferrari 2004

Methods	Title: clinical trial evaluating the peroxide concentration response of whitening strips over 28 days Trial design: randomised, double-blinded, parallel-group clinical study Location: private practice, Italy Language: English Number of centres: 1 Recruitment period: not reported Funding source: Procter & Gamble and Fiji
Participants	Participants: not reported Total number: 37

Ferrari 2004 *(Continued)*

	Inclusion criteria: not reported Exclusion criteria: not Reported Number randomised: 37 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: similar packing Number evaluated: only 34 completed the study among them only 32 – day 7, 29 - day 14, 28 – day 28 were present
Interventions	Total number of intervention groups: 3 1.8% hydrogen peroxide strips 3.3% hydrogen peroxide strips 5.3% hydrogen peroxide strips Duration of treatment: 28 days
Outcomes	Improvement in tooth shade Tooth whitening was characterized by decreased b* (reduction in yellowness) and increased ΔL* (increased brightness)
Notes	Sample size calculation: not reported Adverse effects: oral irritation Health-related quality of life: not reported Key conclusions of the study authors: "Hydrogen peroxide at concentrations ranging from 1.8%-5.3% resulted in significant colour improvement versus baseline as early as Day 7. There was a concentration-response for reduction in yellowness (delta b*) and lightness improvement (deltaL*) at all time points, favouring the higher concentrations. While the concentration-whitening relationship approached a linear response at Day 7, continued treatment resulted in incremental colour improvement. All 3 peroxide concentrations were well tolerated, and no subjects discontinued early due to a treatment-related adverse event" Correspondence required: yes: number of participants per group is not reported, authors have been mailed requesting these data Contact: Marco Ferrari, Piazza Attias 19, Livorno 57120, Italy, ferrarimar@unisi.it

Gambarini 2004

Methods	Title: efficacy and safety assessment of a new liquid tooth whitening gel containing 5.9% hydrogen peroxide Trial design: double-blinded randomised controlled trial Location: University of Rome, Italy Language: English Number of centres: 1

Gambarini 2004 *(Continued)*

	Recruitment period: not reported
	Funding source: not reported
Participants	Participants: 21 to 52 years
	Total number: 30
	Inclusion criteria: Vita shade score of A2 or darker; adults; staining in teeth
	Exclusion criteria: not reported
	Number randomised: 30
	Method of randomisation: not mentioned
	Method of allocation concealment: not mentioned
	Method of blinding: not reported
	Performance/detection bias: not reported
	Number evaluated: 30
Interventions	Total number of intervention groups: 2
	Hydrogen peroxide gel 5.9%
	Placebo
	Duration of treatment: 2 weeks
Outcomes	Tooth colour change
	Sensitivity
	Bleeding on probing
	Gingival recession
Notes	Adverse effects: sensitivity
	Health-related quality of life: not reported
	Key conclusions of the study authors: "5.9% hydrogen peroxide was significantly effective in lightening tooth shade. After only 2 weeks, patients enrolled in the study exhibited an overall mean 4.48-shade improvement from baseline, which was significantly greater than placebo group and far exceeded the ADA minimum requirements to claim "clinical efficacy". In the new Colgate Simply White Clear Whitening Gel group, periodontal health (PI and BOP) improved with time overall. Moreover, dentin hypersensitivity did not significantly increase, and all treatments were generally well tolerated"
	Correspondence required: yes: missing data, standard deviation cannot be calculated as P values have not been reported in the study. Author has been contacted
	Contact: Dr Gianluca Gambarini, ggambarini@tin.it

Gegauff 1993

Methods	Title: evaluating tooth colour change from carbamide peroxide gel
	Trial design: double-blinded randomised controlled trial

Gegauff 1993 *(Continued)*

	Location: Ohio State University, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Ultradent Products, Inc
Participants	Participants: 20 to 27 years. Mean age 22 years Total number: 20 Inclusion criteria: no anterior restorations; history of anterior tooth pain or trauma; recurrent gingival lesions or abnormal variation in tooth colour; adults Exclusion criteria: not reported Number randomised: 20 Method of randomisation: not mentioned Method of allocation concealment: not reported Method of blinding: similar coded syringes Performance/detection bias: not reported Number evaluated: control: n = 17, (3 dropouts)
Interventions	Total number of intervention groups: 2 Carbamide peroxide 10% Placebo gel Duration of treatment: 8 weeks
Outcomes	Tooth colour change: b* (decreased b* indicates reduced yellowness); ΔL* (increased ΔL* is increased brightness) Gingival Index Effect on sulcus depth
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "We found that maxillary canines had a higher lightness change than maxillary incisors. Additionally, the bleaching treatments significantly reduced the yellowness of all the maxillary anterior teeth. However, this reduction was partially reversed" Correspondence required: yes: missing data, mean and standard deviation not reported, authors have been contacted requesting data Contact: Dr Gegauff, College of Dentistry, Ohio State University, 305 West 12th Ave, Columbus 432101241, USA

Gerlach 2004b

Methods	Title: vital bleaching with a thin peroxide gel: the safety and efficacy of a professional-strength hydrogen peroxide whitening strip Trial design: double-blinded, randomised controlled trial Location: not available Language: English Number of centres: not available Recruitment period: not available Funding source: not available
Participants	Participants: adults Total number: 38 Inclusion criteria: not available Exclusion criteria: not available Number randomised: not available Method of randomisation: not available Method of allocation concealment: not available Method of blinding: not available Number evaluated: not available
Interventions	Total number of intervention groups: 2 6% hydrogen peroxide 14% hydrogen peroxide Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade
Notes	Sample size calculation: not available Adverse effects: oral irritation Health-related quality of life: not available Key conclusions of the study authors: "Use of the thin 14% hydrogen peroxide gel strip resulted in greater whitening, including 42% to 49% greater improvement in tooth colour and faster whitening onset than that seen with a 6% hydrogen peroxide whitening strip, without clinical evidence of increased oral-tissue irritation" Not able to retrieve full text Contact: Dr Robert W Gerlach, Hill Top Research, West Palm Beach, Florida, USA, gerlach.rw@pg.com

Guerrero 2007

Methods	Title: clinical response of a professional whitening strip system. A randomised, double-blind, placebo-controlled study
Participants	A total of 30 volunteer students and staff at the National Autonomous University of Mexico
Interventions	6.5% hydrogen peroxide strips Placebo strips
Outcomes	Safety and efficacy of bleaching strips
Notes	Full text not available

Heymann 1998

Methods	Title: clinical evaluation of 2 carbamide peroxide tooth-whitening agents Trial design: blinded-study Location: not available Language: English Number of centres: not available Recruitment period: not available Funding source: not available
Participants	Participants: not available Total number: 51 Inclusion criteria: not available Exclusion criteria: not available Number randomised: not available Method of randomisation: not available Method of allocation concealment: not available Method of blinding: not available Number evaluated: not available
Interventions	Total number of intervention groups: 2 10% carbamide peroxide: 2 different brands Duration of treatment: 1 week
Outcomes	Improvement in tooth shade
Notes	Sample size calculation: not available Adverse effects: tooth sensitivity and gingival irritation Health-related quality of life: not available

Heymann 1998 *(Continued)*

	Key conclusions of the study authors: "Not significant difference in the bleaching was noted between 2 groups. Mild gingival irritation and hypersensitivity was noticed between both the groups"
	Not able to retrieve full text

Kim 2018

Methods	Title: bleaching effects on colour, chemical, and mechanical properties of white spot lesions
	Trial design: randomised, double-blinded, placebo-controlled trial
	Location: not given in abstract
	Language: English
	Number of centres: 1
	Recruitment period: not given in abstract
	Funding source: not given in abstract
Participants	Participants: not reported
	Total number: 40
	Inclusion criteria: not reported in abstract
	Exclusion criteria: not reported in abstract
	Number randomised: 40
	Method of randomisation: not reported in abstract
	Method of allocation concealment: not reported in abstract
	Method of blinding: not reported in abstract
	Number evaluated: not reported in abstract
Interventions	Total number of intervention groups: 5
	5 groups: 2 test groups (strip and paint-on), 2 negative control groups and 1 positive control group (dentist-supervised home bleaching)
	Duration of treatment: 4 weeks
Outcomes	Improvement in tooth shade
Notes	Yet to procure full text for this article

Maran 2018

Methods	Title: tooth sensitivity with a desensitizing-containing at-home bleaching gel - a randomised triple-blind clinical trial
	Trial design: randomised, triple-blinded, placebo-controlled trial
	Location: not given in the abstract

Maran 2018 *(Continued)*

	Language: English Number of centres: 1 Recruitment period: not given in the abstract Funding source: not given in the abstract
Participants	Participants: not reported Total number: 60 Inclusion criteria: not reported in abstract Exclusion criteria: not reported in abstract Number randomised: 60 Method of randomisation: not reported in abstract Method of allocation concealment: not reported in abstract Method of blinding: not reported in abstract Number evaluated: not reported in abstract
Interventions	Total number of intervention groups: 2 Desensitizing-containing (3% potassium nitrate and 0.2% sodium fluoride) and desensitizing-free 10% carbamide peroxide gel Duration of treatment: 21 days
Outcomes	Improvement in tooth shade
Notes	Yet to procure full text for this article

NCT02151058

Methods	Title: a clinical trial to test the effect of a marketed mouthrinse on stain removal Trial design: single-blinded, randomised controlled trial Location: not reported Language: English Number of centres: 1 Recruitment period: not reported Funding source: Johnson & Johnson Consumer and Personal Products Worldwide
Participants	Participants: 18 to 65 years Total number: 225 Inclusion criteria: • able to comprehend and follow the requirements of the study (including availability on scheduled visits) • able to provide written informed consent

NCT02151058 *(Continued)*

	• male or non-pregnant non-lactating • medically acceptable forms of birth control that may be used by the subject and/or his/her partner • able to read and understand the local language • able to follow study procedures; willing for this to be the only investigational product used during this time period; and willing and able to comply with all study procedures and attend the scheduled visits for the duration of the study • subject must have at least 2 natural anterior teeth, each having a mean Lobene composite score of ≥ 1.5 on the facial surfaces as assessed by the investigator Exclusion criteria: • suspected alcohol or substance abuse • females who are pregnant or breastfeeding • known sensitivity or history of significant adverse effects to any of the investigational products • significant unstable or uncontrolled medical condition which may interfere with a subject's participation in the study • participated in tooth stain removal trials in the last 3 months • participation in any other clinical study within 30 days of visit 1 • subjects who are related to those persons involved directly or indirectly with the conduct of this study Number randomised: not reported Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: not reported
Interventions	Total number of intervention groups: 3 Negative control: Colgate® Regular Cavity Protection Experimental: experimental mouthrinse Active comparator: Crest® 3D White MultiCareWhitening Rinse
Outcomes	Reduction in stain
Notes	Sample size calculation: not reported A protocol for a randomised controlled trial. Full text not available Contact: not reported

NCT03217994

Methods	Title: efficacy of 2 teeth whitening gels. A prospective, double-blind, randomised clinical trial with split-mouth design
Participants	Adults without prior tooth whitening treatments, tooth decay, or restorations of the upper front teeth. The patients had tooth colours of A3 or less according to the Vita classical scale
Interventions	37.5% hydrogen peroxide gel to bleach teeth 6% hydrogen peroxide gel to bleach teeth

NCT03217994 *(Continued)*

Outcomes	Change in tooth colour
Notes	A protocol for a randomised controlled trial. Full text not available

Ozcan 2003

Methods	Title: the efficacy of 2 prototype chewing gums for the removal of extrinsic tooth stain Trial design: Double-blinded, randomised controlled trail, parallel design Location: Marmra University, Istanbul, Turkey Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dandy Sakiz ve Sekerleme Sanayi ve Ticaret AS, Istanbul
Participants	Participants: 18 to 24 years. Mean age 20.6 years Total number: 76 Inclusion criteria: healthy Individual; 12 score able anterior teeth; no orthodontic restoration Exclusion criteria: pregnant or lactating women Number randomised: 60 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported Number evaluated: not reported
Interventions	Total number of intervention groups: 2 Group 1: sorbitol powder, maltilol syrup, mannitol, glycerine and flavour, no active ingredients Group 2: sorbitol powder, maltilol syrup, mannitol, glycerine and flavour, sodium tripolyposphate, dicalcium phosphate and sodium bicarbonate 1:4:5 Duration of treatment: 4 weeks
Outcomes	Reduction of stain in teeth and gingiva Gingiva and body were scored by 4-point intensity scale ranging from no stain (0) to heavy stain (3) and a 4-point area scale ranging from no stain (0) to stain covering greater than 2/3 of region (3)
Notes	Sample size calculation: not reported Adverse effects: reported Health-related quality of life: reported Key conclusions of the study authors: "The overall difference between the stain scores after 4-weeks' use of the chewing gums was statistically significant for both test Product A (without active ingredient) and Product B (with active ingredient) with regard to the mean baseline stain scores.

Ozcan 2003 *(Continued)*

	This difference represented a 48% reduction in stain scores for those subjects using Product A, while the reduction was 64% for the subjects using Product B"
	Correspondence required: yes: missing data. Authors have been contacted
	Contact: Assistant Professor Dr Mutlu Ozcan, University of Groningen, Faculty of Medical Sciences, Oral Health Institute, Antonius Deusinglaan 1, 971 3 AV, Groningen, The Netherlands; mutluozcan@hotmail.com

Pohjola 2002

Methods	Title: sensitivity and tooth whitening agents
	Trial design: randomised controlled trial
	Location: Medical College of Georgia
	Language: English
	Number of centres: 1
	Recruitment period: not reported
	Funding source: not reported
Participants	Participants: 18 years old and above
	Total number: 12
	Inclusion criteria: no medical condition; minimal gingival inflammation; no previous history of vital bleaching; A3 shade or above
	Exclusion criteria: active caries
	Number randomised: 12
	Method of randomisation: not reported
	Method of allocation concealment: not reported
	Method of blinding: not reported
	Number evaluated: not reported
Interventions	Total number of intervention groups: 3
	3 brands of commercial product with 10% carbamide peroxide
	Rembrandt Xtra comfort
	Nite White Excel
	Fx product
	Duration of treatment: 2 weeks
Outcomes	Improvement in tooth shade
	Vita shade guide
Notes	Sample size calculation: not reported
	Adverse effects: sensitivity and gingival irritation

Pohjola 2002 *(Continued)*

	Key conclusions of the study authors: "There was no significant difference between the products with respect to improvement in tooth whitening. All 3 products produced sensitivity. Thermal sensitivity was less with Rembrandt Xtra comfort and Nite White Excel"
	Correspondence required: yes: missing data, P-value not reported. Authors have been contacted
	Contact: Dr Randall M Pohjola, rpobjola2mail.mcg.edu

Reinhardt 1993

Methods	Title: a clinical study of nightguard vital bleaching Trial design: double-blinded, randomised controlled clinical trial Location: University of Iowa, USA Language: English Number of centres: 1 Recruitment period: not reported Funding source: Dentmart and Omnii International
Participants	Participants: not reported Total number: 56 Inclusion criteria: not reported Exclusion criteria: patients with significant periodontal disease; internal tooth staining Number randomised: 56 Method of randomisation: not reported Method of allocation concealment: mentioned, but method not reported Method of blinding: not reported Number evaluated: 56
Interventions	Total number of intervention groups: 4 (3 different tray-based brands versus placebo). Intervention with 2 different application regimens for each Proxigei • Overnight n = 9 • 3 hours n = 8 White & Brite • Overnight n = 6 • 3 hours n = 9 Rembrandt Lighten • Overnight n = 8 • 3 hours n = 8 Control

Reinhardt 1993 *(Continued)*

	• Overnight n = 4 • 3 hours n = 4 Duration of treatment: 3 weeks
Outcomes	Improvement in shade: Vita shade guide: lightest to darkest using Munsell Value Gingival Index: 0 = no inflammation; I = inflammation, but no bleeding; 2 = bleeding on probing; and 3 = spontaneous bleeding Plaque Index: 0 = no plaque; 1= plaque detectable; 2 = plaque from interproximal surface to interproximal surface; 3 = plaque on more than half of tooth
Notes	Sample size calculation: not reported Adverse effects: sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "The overnight (1 application) method produced tooth-lightening resulted at least equivalent to those of the multiple application (3-application, 3-hour) method. When Proxigei or Rembrandt was used, overnight and 3-hour replenishment produced similar results. The use of White & Brite overnight also produced results similar to those of Rembrandt and Proxigei. The least effective treatment was White & Brite used with 3-hour replenishment" Correspondence required: yes: the percentage of the active ingredient used in the trial is not clear. Authors contacted Contact: John W Reinhardt, Department of Operative Dentistry, University of Iowa College of Dentistry, Iowa City 52242, USA

Rosenstiel 1996

Methods	Title: randomised clinical trial of the efficacy and safety of a home bleaching procedure Trial design: double-blinded, randomised controlled trial Location: Ohio State University College, Columbus, Ohio, USA Language: English Number of centres: 1 Funding source: Ultradent
Participants	Participants: women: 28.4 years (range of 21 to 44 years), men: 30.1 years (range of 20 to 57 years) Total number: 52 Inclusion criteria: 6 maxillary anterior teeth; free of restoration/caries Exclusion criteria: intrinsic staining; hypoplasia; fluorosis Number randomised: 52 Method of randomisation: not reported Method of allocation concealment: not reported Method of blinding: not reported

Rosenstiel 1996 *(Continued)*

	Number evaluated: 52
Interventions	Total number of intervention groups: 2 10% carbamide peroxide Placebo Duration of treatment: 5 days
Outcomes	Colour change: b (decreased b* indicates reduced yellowness); ΔL* (increased ΔL* is increased brightness) Sulcus depth Vitality Gingival Index
Notes	Sample size calculation: not reported Adverse effects: sensitivity and gingival irritation Health-related quality of life: not reported Key conclusions of the study authors: "The control group significant reduction in mean colour change at the end of 6 months. The mean colour change was more in canines compared to central incisor. Lightness was significantly increased for the active canines but less with central incisors. There was not change in vitality, sulcus depth or Gingival Index score" Correspondence required: yes: missing data, mean and standard deviation not reported. Authors have been mailed requesting for the data. Contact: Dr Stephen F Rosenstiel, Section of Restorative and Prosthetic Dentistry, Ohio State University, College of Dentistry, 305 West 12th Avenue, Columbus, Ohio 43210, USA

Rossi 2018

Methods	Title: tooth colour changes and sensitivity in patients undergoing dental bleaching with 10% hydrogen peroxide using customized trays or strips: a randomised clinical trial Trial design: randomised, double-blinded, placebo-controlled trial Location: not given in the abstract Language: English Number of centres: 1 Recruitment period: not given in the abstract Funding source: not given in the abstract
Participants	Participants: not reported Total number: 50 Inclusion criteria: not reported in abstract Exclusion criteria: not reported in abstract Number randomised: 50

Rossi 2018 *(Continued)*

	Method of randomisation: not reported in abstract
	Method of allocation concealment: not reported in abstract
	Method of blinding: not reported in abstract
	Number evaluated: not reported in abstract
Interventions	Total number of intervention groups: 2
	10% hydrogen peroxide strip versus tray
	Placebo
	Duration of treatment: 14 days
Outcomes	Improvement in tooth shade
Notes	Yet to procure full text for this article

Shin 2010

Methods	Title: the evaluation of clinical efficacy and longevity of home bleaching without combined application of in-office bleaching
	Trial design: randomised controlled trial
	Location: not reported
	Language: Korean
	Number of centres: 1
	Recruitment period: not reported
	Funding source: not reported
Participants	Participants: age 19 to 40 years
	Total number: 28
	Inclusion criteria: mild tooth discolouration; 6 anterior teeth present
	Exclusion criteria: resin filling; porcelain restoration; dental caries; gingivitis and periodontitis
	Number randomised: not reported
	Method of randomisation: not reported
	Method of allocation concealment: not reported
	Method of blinding: not reported
	Number evaluated: not reported
Interventions	Total number of intervention groups: 2
	15% carbamide peroxide tray
	Placebo
	Duration of treatment: 4 weeks

Shin 2010 *(Continued)*

Outcomes	Change in tooth colour: b (decreased b* indicates reduced yellowness); ΔL* (increased ΔL* is increased brightness)
Notes	Sample size calculation: not reported Adverse effects: not reported Health-related quality of life: not reported Key conclusions of the study authors: "Stronger colour change was observed for overall teeth samples in experimental group immediately after treatment (at 4 weeks) compared to ones in control group. There was also a significant difference between baseline and 8 weeks or 12 weeks as the tooth got darker with time) Correspondence required: yes: missing data, number of participants in control and experimental groups not reported. Authors have been mailed requesting for the data Contact: Sung Wun Yang, dentyun@catholic.ac.kr

Sielski 2003

Methods	Randomised, controlled, examiner-blinded, parallel-group clinical study to determine efficacy of tooth-whitening gel when used once daily at night, as compared with a commercially available dentifrice
Participants	75 adults
Interventions	Non-whitening dentifrice only A tooth-whitening gel with a commercially available dentifrice
Outcomes	Change in tooth colour
Notes	Full text not available

Simon 2014

Methods	Title: placebo-controlled clinical trial evaluating 9.5% hydrogen peroxide high-adhesion whitening strips Trial design: parallel, double-blinded, randomised controlled trial Location: University of Tennessee, USA Language: English Number of centres: 1 Funding source: Procter & Gamble
Participants	Participants: 18 to 65 years Total number: 54 Inclusion criteria: 4 teeth which are A2 shade or darker; healthy adults Exclusion criteria: intrinsic staining; tooth sensitivity; orthodontic device

Simon 2014 *(Continued)*

	Number randomised: not mentioned Method of randomisation: not mentioned Method of allocation concealment: not mention Method of blinding: not mentioned Number evaluated: 54
Interventions	Total number of intervention groups: 2 9.5% hydrogen peroxide strips Placebo Duration of treatment: 3 weeks
Outcomes	Tooth colour change: b (decreased b* indicates reduced yellowness); ΔL* (increased ΔL* is increased brightness) Tooth sensitivity
Notes	Sample size calculation: not reported Adverse effects: oral irritation and tooth sensitivity Health-related quality of life: not reported Key conclusions of the study authors: "Experimental 9.5% hydrogen peroxide strip yielded significant tooth whitening relative to a placebo strip as early as after three days of product use" Correspondence required: yes: authors have been contacted for missing data Contact: Dr James F Simon, farrells.2@pg.com

Characteristics of ongoing studies *[ordered by study ID]*

NCT03026725

Trial name or title	Effect of tricalcium phosphate on efficacy and sensitivity with vital tooth whitening using 20% carbamide peroxide
Methods	Randomised controlled trial
Participants	Not given
Interventions	Not given
Outcomes	Improvement in shade
Starting date	2017
Contact information	clinicaltrials.gov/show/nct03026725
Notes	Results not yet reported

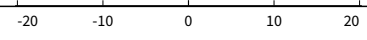
DATA AND ANALYSES

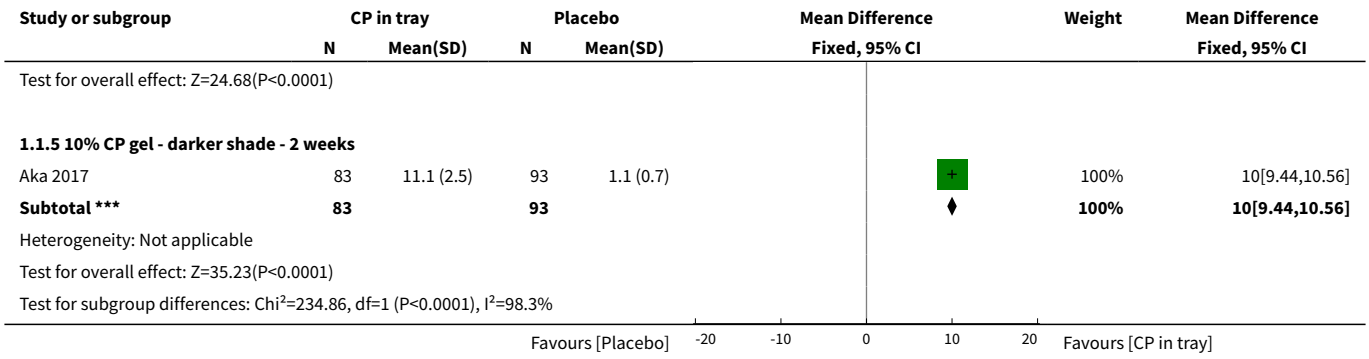
Comparison 1. CP gel in tray versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 5% CP gel - 2 weeks	1	21	Mean Difference (IV, Fixed, 95% CI)	4.56 [1.52, 7.59]
1.2 10% CP gel with desensitiser - 2 weeks	1	37	Mean Difference (IV, Fixed, 95% CI)	4.70 [3.28, 6.12]
1.3 10% CP gel - light shade - 2 weeks	1	179	Mean Difference (IV, Fixed, 95% CI)	4.5 [4.04, 4.96]
1.4 10% CP gel - medium dark shade - 2 weeks	1	172	Mean Difference (IV, Fixed, 95% CI)	6.90 [6.35, 7.45]
1.5 10% CP gel - darker shade - 2 weeks	1	176	Mean Difference (IV, Fixed, 95% CI)	10.0 [9.44, 10.56]

Analysis 1.1. Comparison 1 CP gel in tray versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	CP in tray N	CP in tray Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.1.1 5% CP gel - 2 weeks							
Hyland 2015	10	76.4 (2.4)	11	71.9 (4.5)		100%	4.56[1.52,7.59]
Subtotal ***	**10**		**11**			**100%**	**4.56[1.52,7.59]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.94(P=0)							
1.1.2 10% CP gel with desensitiser - 2 weeks							
Browning 2008	19	14.1 (1.3)	18	9.4 (2.8)		100%	4.7[3.28,6.12]
Subtotal ***	**19**		**18**			**100%**	**4.7[3.28,6.12]**
Heterogeneity: Not applicable							
Test for overall effect: Z=6.49(P<0.0001)							
1.1.3 10% CP gel - light shade - 2 weeks							
Aka 2017	89	5.9 (2)	90	1.4 (0.9)		100%	4.5[4.04,4.96]
Subtotal ***	**89**		**90**			**100%**	**4.5[4.04,4.96]**
Heterogeneity: Not applicable							
Test for overall effect: Z=19.37(P<0.0001)							
1.1.4 10% CP gel - medium dark shade - 2 weeks							
Aka 2017	81	8.1 (2.4)	91	1.2 (0.8)		100%	6.9[6.35,7.45]
Subtotal ***	**81**		**91**			**100%**	**6.9[6.35,7.45]**
Heterogeneity: Not applicable							

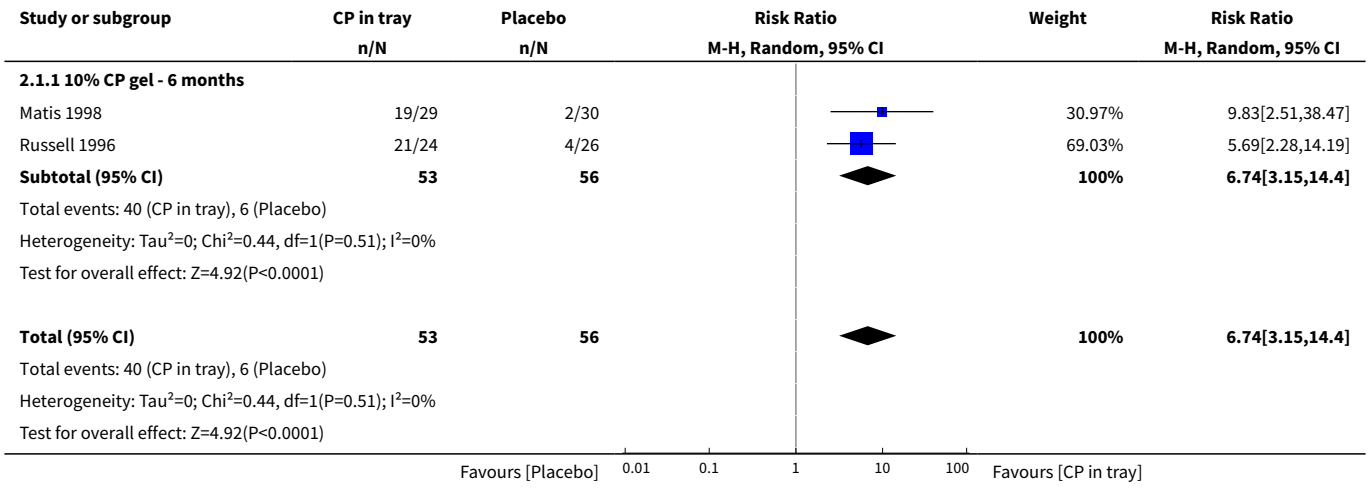




Comparison 2. CP gel in tray versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2	109	Risk Ratio (M-H, Random, 95% CI)	6.74 [3.15, 14.40]
1.1 10% CP gel - 6 months	2	109	Risk Ratio (M-H, Random, 95% CI)	6.74 [3.15, 14.40]

Analysis 2.1. Comparison 2 CP gel in tray versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

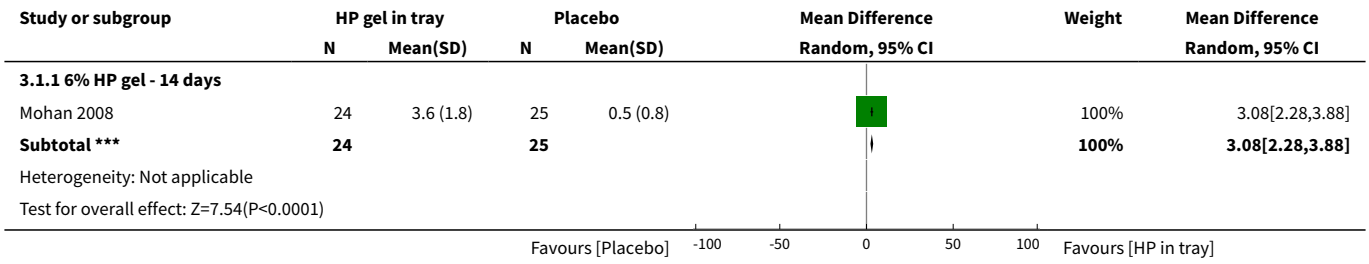


Comparison 3. HP gel in tray versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 6% HP gel - 14 days	1	49	Mean Difference (IV, Random, 95% CI)	3.08 [2.28, 3.88]

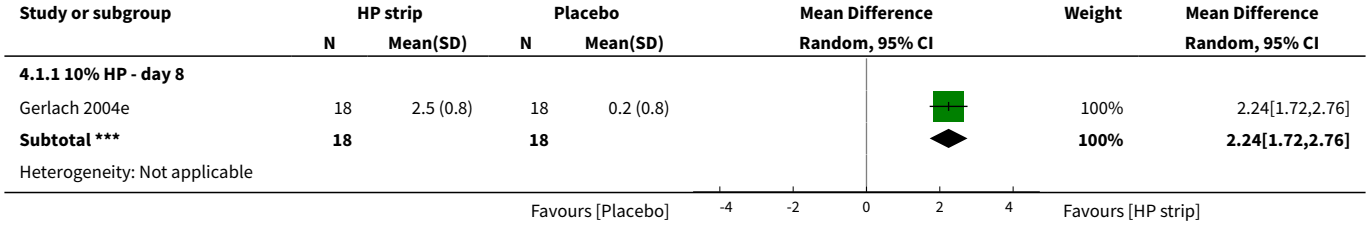
Analysis 3.1. Comparison 3 HP gel in tray versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

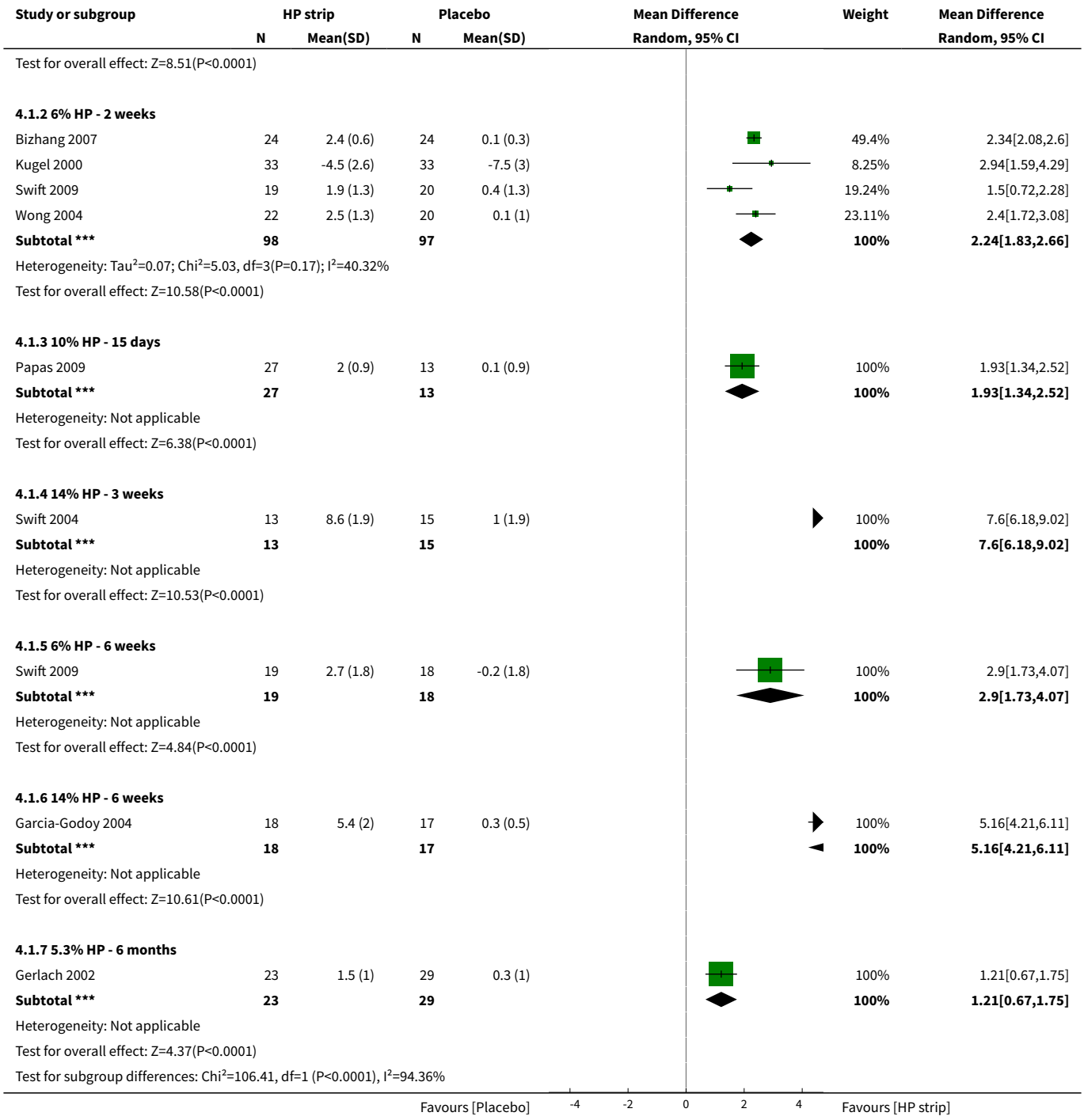


Comparison 4. HP strip versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 10% HP - day 8	1	36	Mean Difference (IV, Random, 95% CI)	2.24 [1.72, 2.76]
1.2 6% HP - 2 weeks	4	195	Mean Difference (IV, Random, 95% CI)	2.24 [1.83, 2.66]
1.3 10% HP - 15 days	1	40	Mean Difference (IV, Random, 95% CI)	1.93 [1.34, 2.52]
1.4 14% HP - 3 weeks	1	28	Mean Difference (IV, Random, 95% CI)	7.6 [6.18, 9.02]
1.5 6% HP - 6 weeks	1	37	Mean Difference (IV, Random, 95% CI)	2.90 [1.73, 4.07]
1.6 14% HP - 6 weeks	1	35	Mean Difference (IV, Random, 95% CI)	5.16 [4.21, 6.11]
1.7 5.3% HP - 6 months	1	52	Mean Difference (IV, Random, 95% CI)	1.21 [0.67, 1.75]

Analysis 4.1. Comparison 4 HP strip versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.





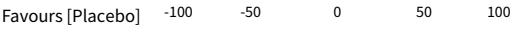
Comparison 5. CP paint-on gel versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 18% CP paint-on gel - 3 weeks	1	77	Mean Difference (IV, Random, 95% CI)	3.50 [3.12, 3.88]

Analysis 5.1. Comparison 5 CP paint-on gel versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	CP paint-on N	CP paint-on Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.1.1 18% CP paint-on gel - 3 weeks							
Nathoo 2002	38	3.8 (1.1)	39	0.3 (0.5)		100%	3.5[3.12,3.88]
Subtotal ***	**38**		**39**			**100%**	**3.5[3.12,3.88]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=18.11(P<0.0001)							

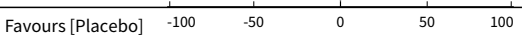


Comparison 6. HP paint-on gel versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 6% HP - 2 weeks	2	148	Std. Mean Difference (IV, Random, 95% CI)	0.67 [0.19, 1.14]

Analysis 6.1. Comparison 6 HP paint-on gel versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	HP paint-on N	HP paint-on Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
6.1.1 6% HP - 2 weeks							
Collins 2004a	58	1 (1.3)	59	0.4 (1.3)		70.33%	0.51[0.14,0.88]
Xu 2007	15	0.6 (0.6)	16	-0.1 (0.7)		29.67%	1.04[0.28,1.8]
Subtotal ***	**73**		**75**			**100%**	**0.67[0.19,1.14]**
Heterogeneity: Tau²=0.05; Chi²=1.52, df=1(P=0.22); I²=34.07%							
Test for overall effect: Z=2.76(P=0.01)							

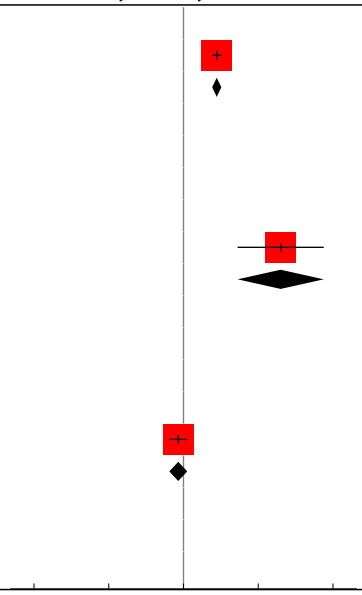


Comparison 7. Chewing gum SHMP versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	3		Mean Difference (Random, 95% CI)	Subtotals only
1.1 7.5% SHMP gum - 2 days	1	37	Mean Difference (Random, 95% CI)	0.89 [0.77, 1.01]
1.2 5.6% SHMP gum - 3 days	1	20	Mean Difference (Random, 95% CI)	2.6 [1.45, 3.75]
1.3 4% SHMP gum - 12 weeks	1	108	Mean Difference (Random, 95% CI)	-0.14 [-0.38, 0.10]

Analysis 7.1. Comparison 7 Chewing gum SHMP versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	SHMP chewing gum N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
7.1.1 7.5% SHMP gum - 2 days						
Biesbrock 2004	19	18	0.9 (0.063)		100%	0.89[0.77,1.01]
Subtotal (95% CI)					**100%**	**0.89[0.77,1.01]**
Heterogeneity: Not applicable						
Test for overall effect: Z=14.24(P<0.0001)						
7.1.2 5.6% SHMP gum - 3 days						
Walters 2004	10	10	2.6 (0.588)		100%	2.6[1.45,3.75]
Subtotal (95% CI)					**100%**	**2.6[1.45,3.75]**
Heterogeneity: Not applicable						
Test for overall effect: Z=4.42(P<0.0001)						
7.1.3 4% SHMP gum - 12 weeks						
Porciani 2006	54	54	-0.1 (0.123)		100%	-0.14[-0.38,0.1]
Subtotal (95% CI)					**100%**	**-0.14[-0.38,0.1]**
Heterogeneity: Not applicable						
Test for overall effect: Z=1.14(P=0.25)						
Test for subgroup differences: Chi^2=66.54, df=1 (P<0.0001), I^2=96.99%						

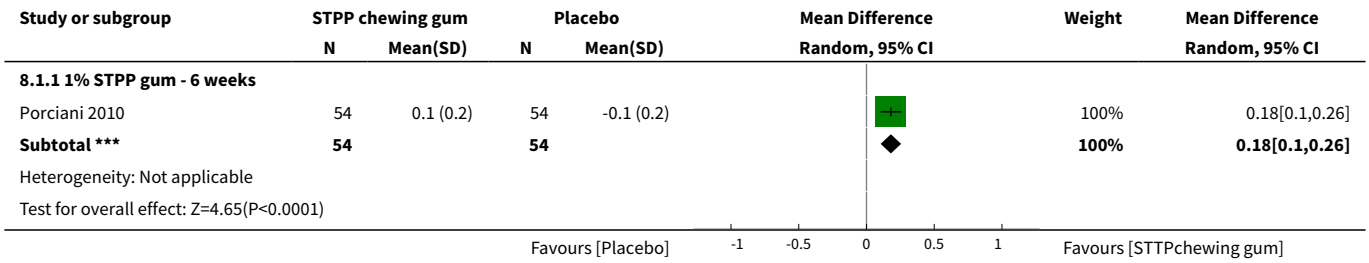


Comparison 8. Chewing gum STPP versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 1% STPP gum - 6 weeks	1	108	Mean Difference (IV, Random, 95% CI)	0.18 [0.10, 0.26]

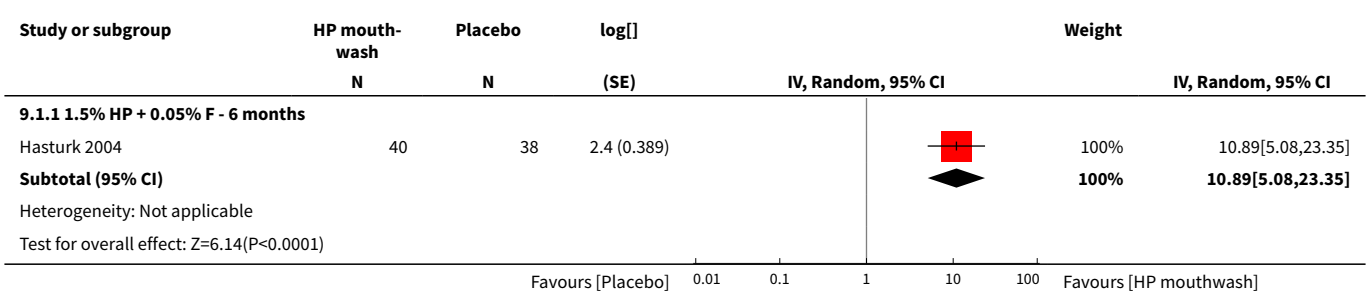
Analysis 8.1. Comparison 8 Chewing gum STPP versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.



Comparison 9. HP mouthwash versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		(Random, 95% CI)	Subtotals only
1.1 1.5% HP + 0.05% F - 6 months	1	78	(Random, 95% CI)	10.89 [5.08, 23.35]

Analysis 9.1. Comparison 9 HP mouthwash versus placebo, Outcome 1 Tooth whitening - assessed by the dentist.

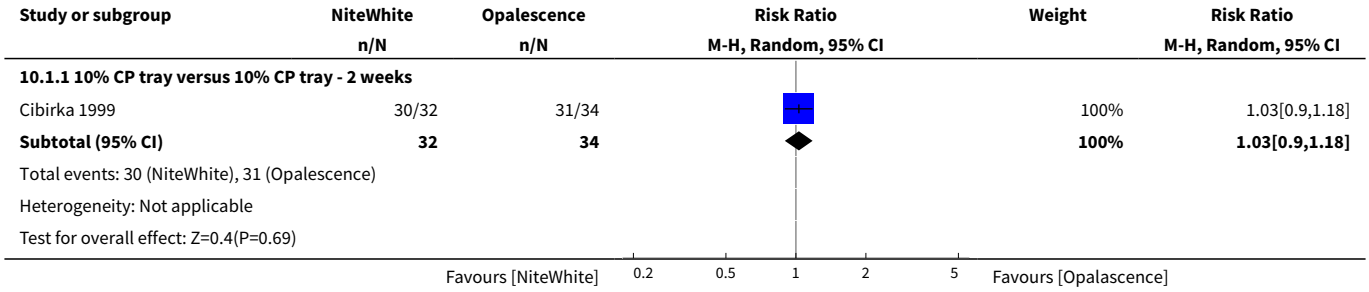


Comparison 10. CP tray versus CP tray

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 10% CP tray versus 10% CP tray - 2 weeks	1	66	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.90, 1.18]

Analysis 10.1. Comparison 10 CP tray versus CP tray, Outcome 1 Tooth whitening - assessed by the dentist.



Comparison 11. CP tray versus CP tray

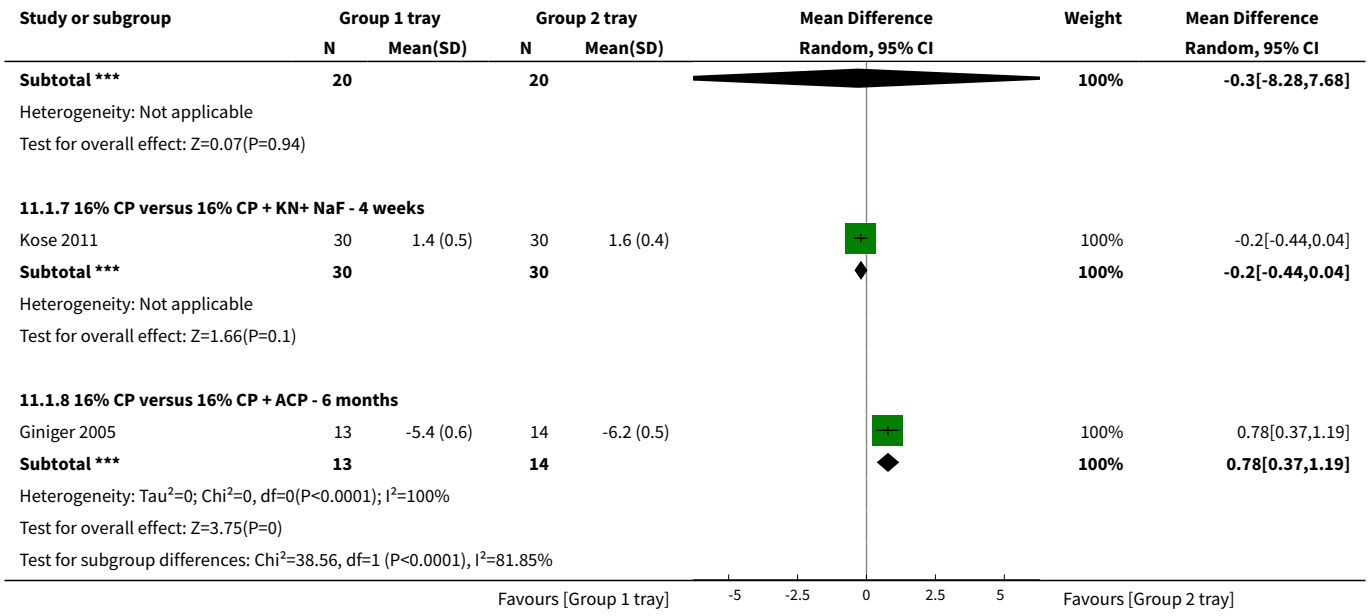
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 5% CP versus 10% CP - 1 week	1	58	Mean Difference (IV, Random, 95% CI)	-0.38 [-5.55, 4.79]
1.2 5% CP versus 10% CP - 2 weeks	1	21	Mean Difference (IV, Random, 95% CI)	0.41 [-2.17, 2.98]
1.3 10% CP Colgate Platinum versus 10% CP Rembrandt Lighten - 2 weeks	2	88	Mean Difference (IV, Random, 95% CI)	-1.92 [-2.80, -1.03]
1.4 10% CP versus 28% CP - 1 year follow-up	1	20	Mean Difference (IV, Random, 95% CI)	-3.30 [-8.71, 2.11]
1.5 10% CP versus 16% CP - 2-year follow-up	1	81	Mean Difference (IV, Random, 95% CI)	1.20 [-0.35, 2.75]
1.6 30% CP versus 30% CP + KN - 10 days	1	40	Mean Difference (IV, Random, 95% CI)	-0.30 [-8.28, 7.68]
1.7 16% CP versus 16% CP + KN+ NaF - 4 weeks	1	60	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.44, 0.04]
1.8 16% CP versus 16% CP + ACP - 6 months	1	27	Mean Difference (IV, Random, 95% CI)	0.78 [0.37, 1.19]
2 Tooth whitening - assessed by the dentist	2		Mean Difference (Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 10% CP Polanight versus 10% CP Opalescence - 2 weeks	1	116	Mean Difference (Fixed, 95% CI)	1.46 [0.13, 2.79]
2.2 10% CP versus 15% CP tetracycline-stained teeth - 5 years	1	58	Mean Difference (Fixed, 95% CI)	-1.47 [-3.56, 0.62]
3 Tooth whitening - reported by the patient	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 10% CP versus 17% CP - Patient-contentment - 3 weeks	1	20	Mean Difference (IV, Fixed, 95% CI)	2.60 [2.57, 2.63]

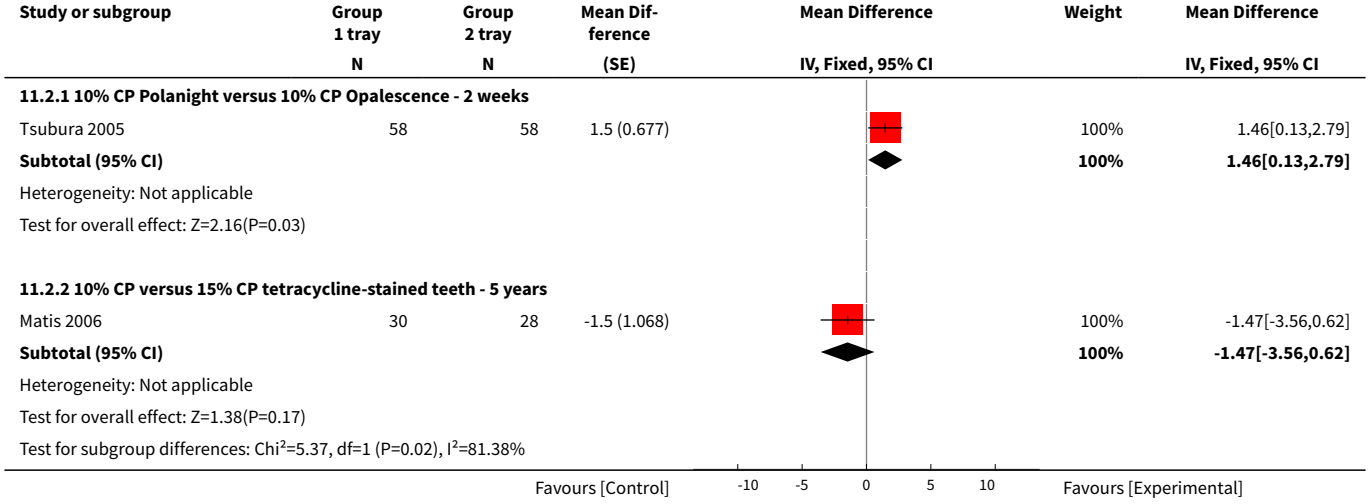
Analysis 11.1. Comparison 11 CP tray versus CP tray, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	Group 1 tray N	Group 1 tray Mean(SD)	Group 2 tray N	Group 2 tray Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
11.1.1 5% CP versus 10% CP - 1 week							
Nathoo 2001	29	-4.4 (10.2)	29	-4 (9.9)		100%	-0.38[-5.55,4.79]
Subtotal ***	**29**		**29**			**100%**	**-0.38[-5.55,4.79]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.14(P=0.89)							
11.1.2 5% CP versus 10% CP - 2 weeks							
Hyland 2015	10	-76.4 (2.4)	11	-76.8 (3.5)		100%	0.41[-2.17,2.98]
Subtotal ***	**10**		**11**			**100%**	**0.41[-2.17,2.98]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.31(P=0.76)							
11.1.3 10% CP Colgate Platinum versus 10% CP Rembrandt Lighten - 2 weeks							
Kowitz 1994	24	-3.4 (1.5)	24	-1.7 (1.3)		75.5%	-1.66[-2.44,-0.88]
Nathoo 1994	20	-3.8 (3.1)	20	-1.1 (2.3)		24.5%	-2.71[-4.37,-1.05]
Subtotal ***	**44**		**44**			**100%**	**-1.92[-2.8,-1.03]**
Heterogeneity: Tau^2=0.11; Chi^2=1.25, df=1(P=0.26); I^2=20.3%							
Test for overall effect: Z=4.25(P<0.0001)							
11.1.4 10% CP versus 28% CP - 1 year follow-up							
Turkun 2010	10	-80.9 (6.6)	10	-77.6 (5.7)		100%	-3.3[-8.71,2.11]
Subtotal ***	**10**		**10**			**100%**	**-3.3[-8.71,2.11]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.2(P=0.23)							
11.1.5 10% CP versus 16% CP - 2-year follow-up							
Meireles 2010	42	-81 (3.8)	39	-82.2 (3.3)		100%	1.2[-0.35,2.75]
Subtotal ***	**42**		**39**			**100%**	**1.2[-0.35,2.75]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.52(P=0.13)							
11.1.6 30% CP versus 30% CP + KN - 10 days							
Gallo 2009	20	17 (6.5)	20	17.3 (17)		100%	-0.3[-8.28,7.68]

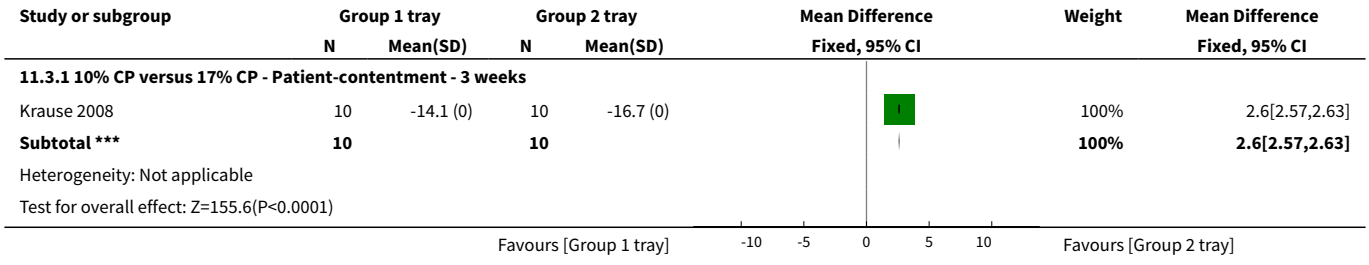
Favours [Group 1 tray] Favours [Group 2 tray]



Analysis 11.2. Comparison 11 CP tray versus CP tray, Outcome 2 Tooth whitening - assessed by the dentist.



Analysis 11.3. Comparison 11 CP tray versus CP tray, Outcome 3 Tooth whitening - reported by the patient.

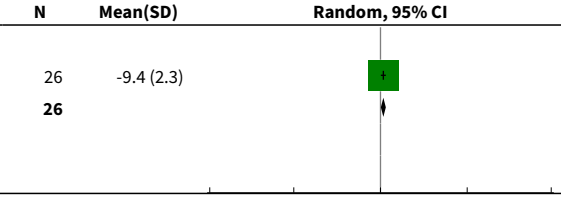


Comparison 12. CP tray versus CP tray

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 10% CP versus 15% CP - 2 weeks	1	52	Mean Difference (IV, Random, 95% CI)	1.65 [0.22, 3.08]
2 Tooth whitening - assessed by the dentist	1	25	Mean Difference (Fixed, 95% CI)	2.22 [1.29, 3.15]
2.1 10% CP versus 15% CP - 2 weeks	1	25	Mean Difference (Fixed, 95% CI)	2.22 [1.29, 3.15]
3 Tooth whitening - assessed by the dentist	2	58	Std. Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.20, 0.84]
3.1 10% CP versus 10% CP + KN + NaF - 2 weeks	2	58	Std. Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.20, 0.84]

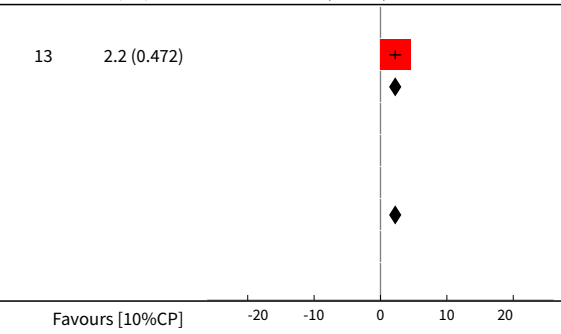
Analysis 12.1. Comparison 12 CP tray versus CP tray, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	Group 1 tray N	Group 1 tray Mean(SD)	Group 2 tray N	Group 2 tray Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
12.1.1 10% CP versus 15% CP - 2 weeks							
Kihn 2000	26	-7.7 (3)	26	-9.4 (2.3)		100%	1.65[0.22,3.08]
Subtotal ***	**26**		**26**			**100%**	**1.65[0.22,3.08]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.26(P=0.02)							

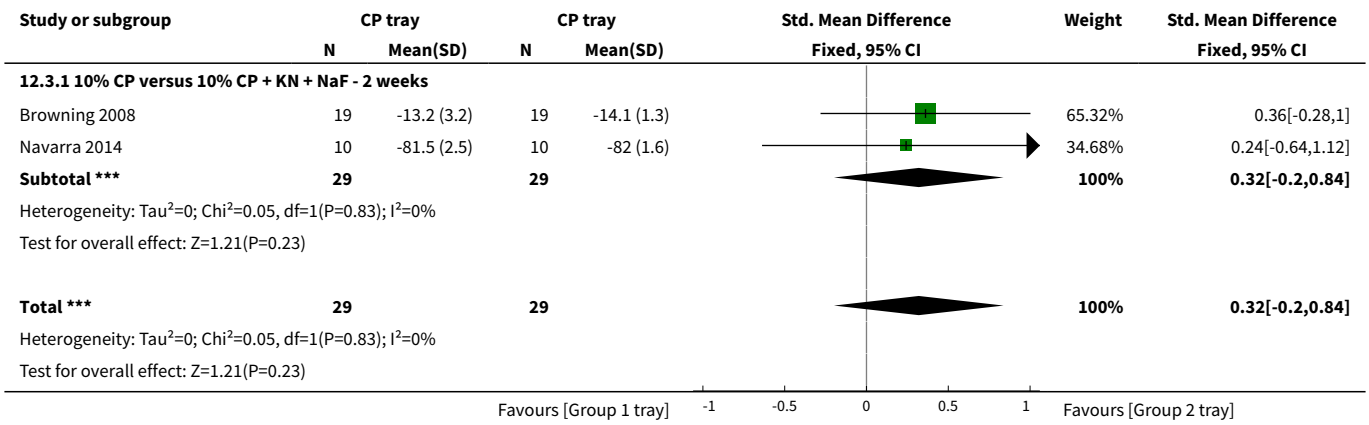


Analysis 12.2. Comparison 12 CP tray versus CP tray, Outcome 2 Tooth whitening - assessed by the dentist.

Study or subgroup	10% CP N	15% CP N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
12.2.1 10% CP versus 15% CP - 2 weeks						
Matis 2000	12	13	2.2 (0.472)		100%	2.22[1.29,3.15]
Subtotal (95% CI)					**100%**	**2.22[1.29,3.15]**
Heterogeneity: Not applicable						
Test for overall effect: Z=4.7(P<0.0001)						
Total (95% CI)					**100%**	**2.22[1.29,3.15]**
Heterogeneity: Not applicable						
Test for overall effect: Z=4.7(P<0.0001)						



Analysis 12.3. Comparison 12 CP tray versus CP tray, Outcome 3 Tooth whitening - assessed by the dentist.

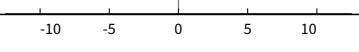


Comparison 13. CP tray versus HP tray

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 20% CP versus 7.5% HP - 12 days	1	56	Mean Difference (IV, Random, 95% CI)	-0.99 [-2.32, 0.34]
1.2 10% CP versus 7.5% HP - 2 weeks	1	48	Mean Difference (IV, Random, 95% CI)	-1.00 [-2.86, 0.86]
1.3 20% CP versus 9% HP - 2 weeks	1	37	Mean Difference (IV, Random, 95% CI)	-0.58 [-8.01, 6.85]
1.4 10% CP versus 6% HP - 2 weeks - medium dark and light shade	1	349	Mean Difference (IV, Random, 95% CI)	-2.22 [-2.63, -1.81]
1.5 10% CP versus 6% HP - 2 weeks - darker shade	1	164	Mean Difference (IV, Random, 95% CI)	-4.3 [-5.02, -3.58]
1.6 20% CP versus 7.5% HP - 12 weeks	1	24	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.40, -0.10]
2 Tooth whitening - assessed by the dentist	1		Mean Difference (Fixed, 95% CI)	Subtotals only
2.1 20% CP versus 7.5% HP - 12 weeks	1	24	Mean Difference (Fixed, 95% CI)	0.25 [0.10, 0.40]

Analysis 13.1. Comparison 13 CP tray versus HP tray, Outcome 1 Tooth whitening - assessed by the dentist.

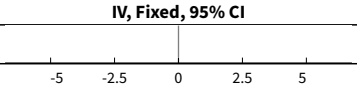
Study or subgroup	CP tray N	CP tray Mean(SD)	HP tray N	HP tray Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
13.1.1 20% CP versus 7.5% HP - 12 days							
Ziebolz 2007	27	-2.6 (3.1)	29	-1.6 (1.8)		100%	-0.99[-2.32,0.34]
Subtotal ***	**27**		**29**			**100%**	**-0.99[-2.32,0.34]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.46(P=0.14)							
13.1.2 10% CP versus 7.5% HP - 2 weeks							
Alonso 2014	24	3.4 (3.7)	24	4.4 (2.8)		100%	-1[-2.86,0.86]
Subtotal ***	**24**		**24**			**100%**	**-1[-2.86,0.86]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.06(P=0.29)							
13.1.3 20% CP versus 9% HP - 2 weeks							
Delgado 2007	16	-7 (10.7)	21	-6.4 (12.3)		100%	-0.58[-8.01,6.85]
Subtotal ***	**16**		**21**			**100%**	**-0.58[-8.01,6.85]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.15(P=0.88)							
13.1.4 10% CP versus 6% HP - 2 weeks - medium dark and light shade							
Aka 2017	89	-5.9 (2)	91	-3.8 (1.6)		60.54%	-2.1[-2.63,-1.57]
Aka 2017	81	-8.1 (2.4)	88	-5.7 (1.9)		39.46%	-2.4[-3.06,-1.74]
Subtotal ***	**170**		**179**			**100%**	**-2.22[-2.63,-1.81]**
Heterogeneity: Tau^2=0; Chi^2=0.49, df=1(P=0.49); I^2=0%							
Test for overall effect: Z=10.55(P<0.0001)							
13.1.5 10% CP versus 6% HP - 2 weeks - darker shade							
Aka 2017	83	-11.1 (2.5)	81	-6.8 (2.2)		100%	-4.3[-5.02,-3.58]
Subtotal ***	**83**		**81**			**100%**	**-4.3[-5.02,-3.58]**
Heterogeneity: Not applicable							
Test for overall effect: Z=11.7(P<0.0001)							
13.1.6 20% CP versus 7.5% HP - 12 weeks							
Mokhlis 2000	13	-2 (0.2)	11	-1.7 (0.2)		100%	-0.25[-0.4,-0.1]
Subtotal ***	**13**		**11**			**100%**	**-0.25[-0.4,-0.1]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.21(P=0)							
Test for subgroup differences: Chi^2=181.01, df=1 (P<0.0001), I^2=97.24%							



Analysis 13.2. Comparison 13 CP tray versus HP tray, Outcome 2 Tooth whitening - assessed by the dentist.

Study or subgroup	CP tray N	HP tray N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
13.2.1 20% CP versus 7.5% HP - 12 weeks						
Mokhlis 2000	13	11	0.3 (0.078)		100%	0.25[0.1,0.4]
Subtotal (95% CI)					**100%**	**0.25[0.1,0.4]**
Heterogeneity: Not applicable						

Study or subgroup	CP tray N	HP tray N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
Test for overall effect: Z=3.21(P=0)						



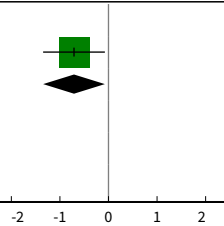
Favours [7.5% HP] Favours [20% CP]

Comparison 14. HP strip versus CP tray

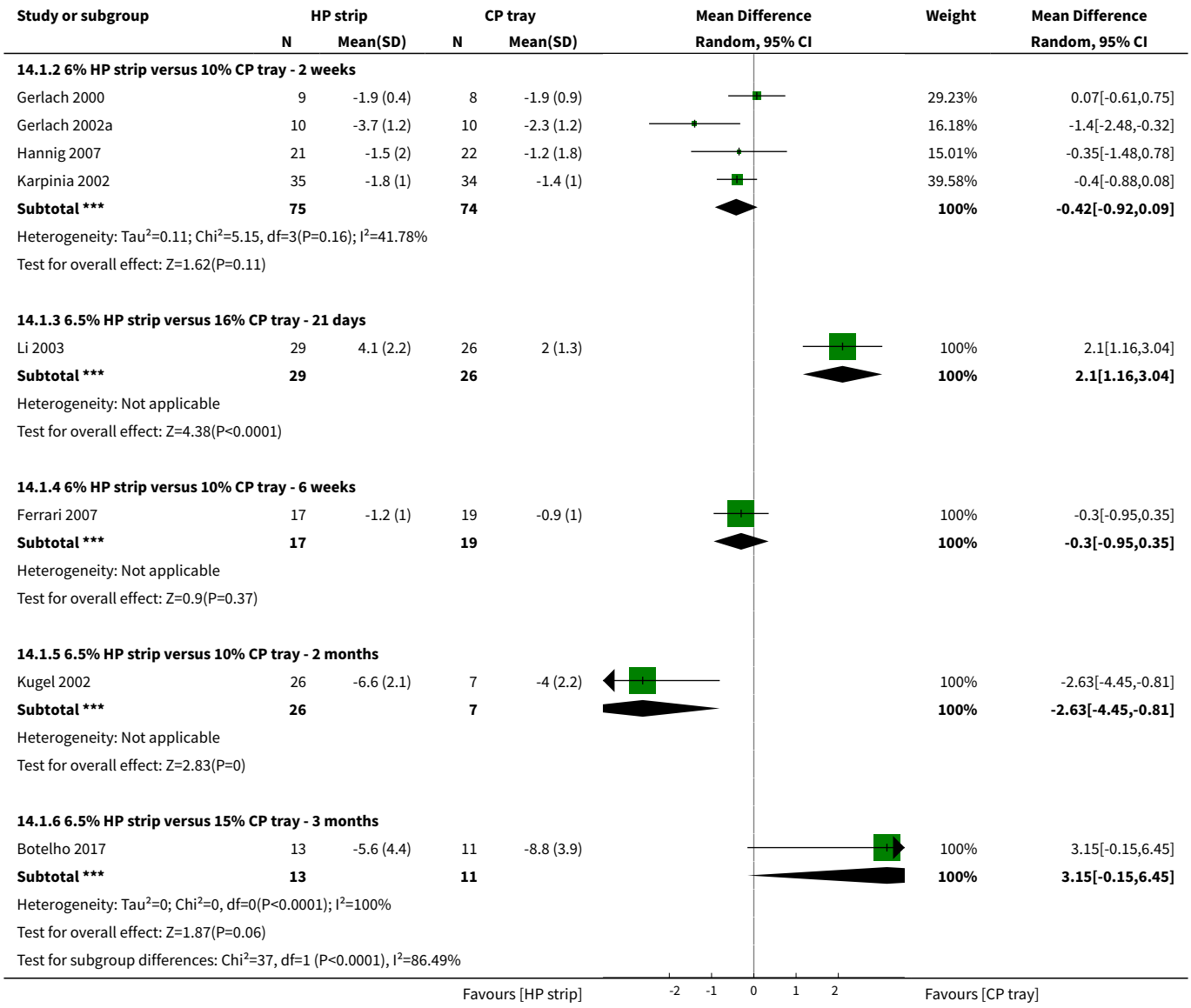
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 6% HP strip versus 5% CP + 5% KN tray - 1 week	1	32	Mean Difference (IV, Random, 95% CI)	-0.71 [-1.35, -0.07]
1.2 6% HP strip versus 10% CP tray - 2 weeks	4	149	Mean Difference (IV, Random, 95% CI)	-0.42 [-0.92, 0.09]
1.3 6.5% HP strip versus 16% CP tray - 21 days	1	55	Mean Difference (IV, Random, 95% CI)	2.10 [1.16, 3.04]
1.4 6% HP strip versus 10% CP tray - 6 weeks	1	36	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.95, 0.35]
1.5 6.5% HP strip versus 10% CP tray - 2 months	1	33	Mean Difference (IV, Random, 95% CI)	-2.63 [-4.45, -0.81]
1.6 6.5% HP strip versus 15% CP tray - 3 months	1	24	Mean Difference (IV, Random, 95% CI)	3.15 [-0.15, 6.45]
2 Tooth whitening - assessed by the dentist	1		Mean Difference (Fixed, 95% CI)	Subtotals only
2.1 14% HP strip versus 35% CP tray - 30 days	1	24	Mean Difference (Fixed, 95% CI)	0.58 [-0.61, 1.77]
3 Tooth whitening - reported by the patient	1	43	Mean Difference (IV, Fixed, 95% CI)	-0.41 [-2.05, 1.23]

Analysis 14.1. Comparison 14 HP strip versus CP tray, Outcome 1 Tooth whitening - assessed by the dentist.

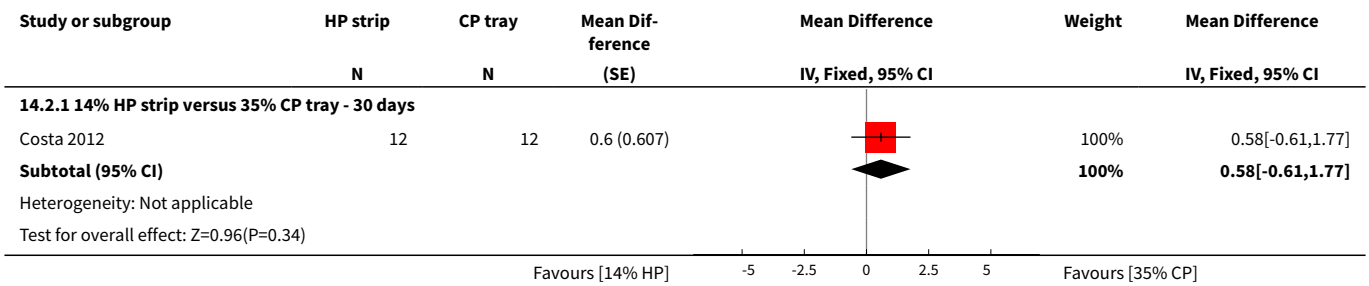
Study or subgroup	HP strip N	HP strip Mean(SD)	CP tray N	CP tray Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
14.1.1 6% HP strip versus 5% CP + 5% KN tray - 1 week							
Gerlach 2002b	15	-1.9 (0.9)	17	-1.2 (0.9)		100%	-0.71[-1.35,-0.07]
Subtotal ***	**15**		**17**			**100%**	**-0.71[-1.35,-0.07]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.19(P=0.03)							



Favours [HP strip] Favours [CP tray]

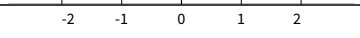


Analysis 14.2. Comparison 14 HP strip versus CP tray, Outcome 2 Tooth whitening - assessed by the dentist.



Analysis 14.3. Comparison 14 HP strip versus CP tray, Outcome 3 Tooth whitening - reported by the patient.

Study or subgroup	HP strip N	HP strip Mean(SD)	CP tray N	CP tray Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hannig 2007	21	4.1 (2.7)	22	4.6 (2.7)		100%	-0.41[-2.05,1.23]
Total ***	**21**		**22**			**100%**	**-0.41[-2.05,1.23]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=0.49(P=0.62)							



Comparison 15. HP strip versus HP tray

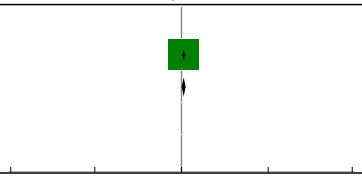
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 14% HP strip versus 9.5% HP tray - 22 days	1	29	Mean Difference (IV, Random, 95% CI)	-1.4 [-2.35, -0.45]
1.2 5.3% HP strip versus 5% HP tray - 18 months	1	28	Mean Difference (IV, Random, 95% CI)	-0.06 [-2.36, 2.24]
2 Patient comfort	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 5.3% HP strip versus 5% HP tray	1	28	Mean Difference (IV, Fixed, 95% CI)	1.27 [0.13, 2.41]

Analysis 15.1. Comparison 15 HP strip versus HP tray, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	HP strip N	HP strip Mean(SD)	HP tray N	HP tray Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
15.1.1 14% HP strip versus 9.5% HP tray - 22 days							
Gerlach 2004	14	-3.1 (1.3)	15	-1.7 (1.3)		100%	-1.4[-2.35,-0.45]
Subtotal ***	**14**		**15**			**100%**	**-1.4[-2.35,-0.45]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.9(P=0)							
15.1.2 5.3% HP strip versus 5% HP tray - 18 months							
Auschill 2012	14	-6.4 (2.7)	14	-6.3 (3.5)		100%	-0.06[-2.36,2.24]
Subtotal ***	**14**		**14**			**100%**	**-0.06[-2.36,2.24]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.05(P=0.96)							
Test for subgroup differences: Chi²=1.12, df=1 (P=0.29), I²=10.34%							

Analysis 15.2. Comparison 15 HP strip versus HP tray, Outcome 2 Patient comfort.

Study or subgroup	HP strip N	HP strip Mean(SD)	HP tray N	HP tray Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
15.2.1 5.3% HP strip versus 5% HP tray							
Auschill 2012	14	3.5 (1.6)	14	2.2 (1.5)		100%	1.27[0.13,2.41]
Subtotal ***	**14**		**14**			**100%**	**1.27[0.13,2.41]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.19(P=0.03)							



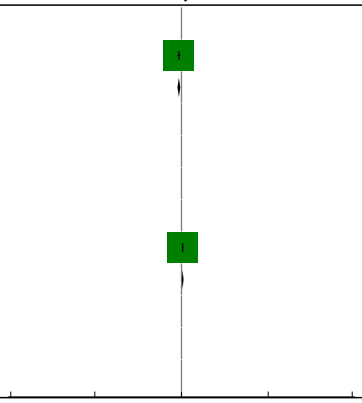
Favours [HP strip] Favours [HP tray]

Comparison 16. HP strip versus HP strip

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 9.5% HP strip versus 10% HP strip - day 9	1	29	Mean Difference (IV, Random, 95% CI)	-1.5 [-2.33, -0.67]
1.2 6% HP strip versus 10% HP strip - 15 days	1	35	Mean Difference (IV, Random, 95% CI)	0.68 [0.16, 1.20]

Analysis 16.1. Comparison 16 HP strip versus HP strip, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	Group 1 HP N	Group 1 HP Mean(SD)	Group 2 HP N	Group 2 HP Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
16.1.1 9.5% HP strip versus 10% HP strip - day 9							
Oliveira 2013	14	-3.8 (1.1)	15	-2.3 (1.2)		100%	-1.5[-2.33,-0.67]
Subtotal ***	**14**		**15**			**100%**	**-1.5[-2.33,-0.67]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.54(P=0)							
16.1.2 6% HP strip versus 10% HP strip - 15 days							
Shahidi 2005	19	-2.3 (0.8)	16	-3 (0.8)		100%	0.68[0.16,1.2]
Subtotal ***	**19**		**16**			**100%**	**0.68[0.16,1.2]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.58(P=0.01)							
Test for subgroup differences: Chi^2=19.12, df=1 (P<0.0001), I^2=94.77%							

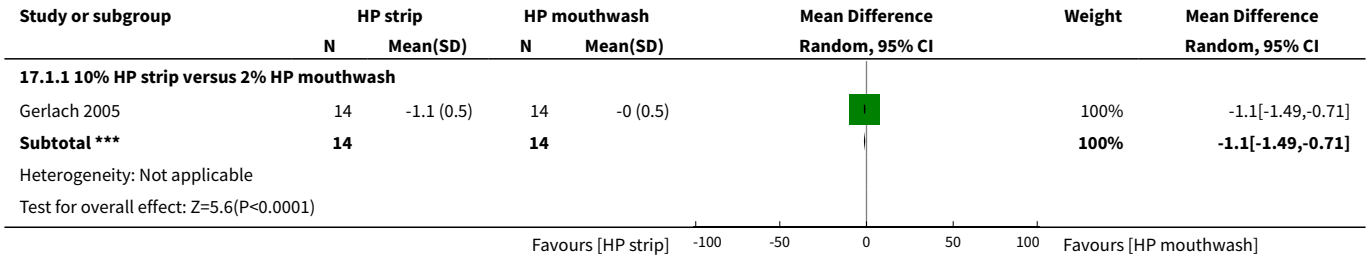


Favours [Group 1 HP] Favours [Group 2 HP]

Comparison 17. HP strip versus HP mouthwash

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 10% HP strip versus 2% HP mouthwash	1	28	Mean Difference (IV, Random, 95% CI)	-1.10 [-1.49, -0.71]

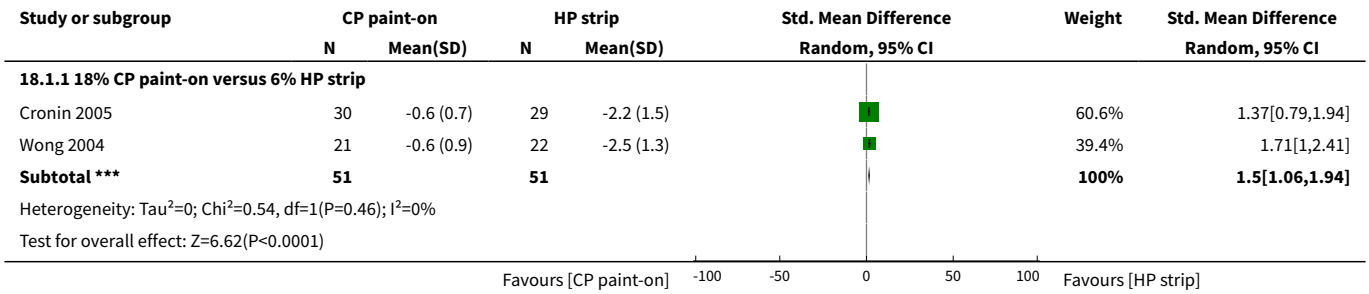
Analysis 17.1. Comparison 17 HP strip versus HP mouthwash, Outcome 1 Tooth whitening - assessed by the dentist.



Comparison 18. CP paint-on versus HP strip

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 18% CP paint-on versus 6% HP strip	2	102	Std. Mean Difference (IV, Random, 95% CI)	1.50 [1.06, 1.94]

Analysis 18.1. Comparison 18 CP paint-on versus HP strip, Outcome 1 Tooth whitening - assessed by the dentist.

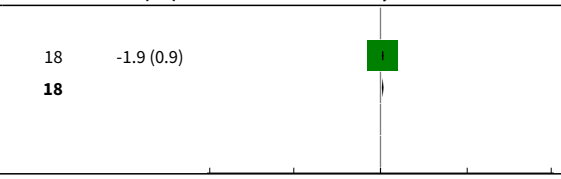


Comparison 19. HP paint-on versus HP strip

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 5.9% HP paint-on versus 6% HP strip	1	33	Mean Difference (IV, Random, 95% CI)	1.28 [0.77, 1.79]
2 Tooth whitening - assessed by the dentist	1		Mean Difference (Fixed, 95% CI)	Subtotals only
2.1 5.9% HP paint-on versus 5.9% HP strip	1	40	Mean Difference (Fixed, 95% CI)	2.7 [2.08, 3.32]
3 Tooth whitening - reported by the patient	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 5.9% HP paint-on versus 5.9% HP strip	1	40	Mean Difference (IV, Fixed, 95% CI)	-0.25 [-1.88, 1.38]

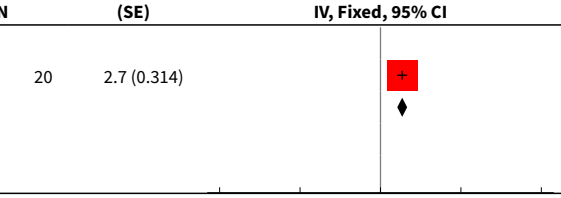
Analysis 19.1. Comparison 19 HP paint-on versus HP strip, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	HP paint-on N	HP paint-on Mean(SD)	HP strip N	HP strip Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
19.1.1 5.9% HP paint-on versus 6% HP strip							
Xu 2007	15	-0.6 (0.6)	18	-1.9 (0.9)		100%	1.28[0.77,1.79]
Subtotal ***	**15**		**18**			**100%**	**1.28[0.77,1.79]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.97(P<0.0001)							



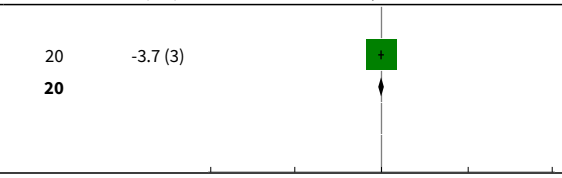
Analysis 19.2. Comparison 19 HP paint-on versus HP strip, Outcome 2 Tooth whitening - assessed by the dentist.

Study or subgroup	HP paint-on N	HP strip N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
19.2.1 5.9% HP paint-on versus 5.9% HP strip						
Auschill 2007	20	20	2.7 (0.314)		100%	2.7[2.08,3.32]
Subtotal (95% CI)					**100%**	**2.7[2.08,3.32]**
Heterogeneity: Not applicable						
Test for overall effect: Z=8.6(P<0.0001)						



Analysis 19.3. Comparison 19 HP paint-on versus HP strip, Outcome 3 Tooth whitening - reported by the patient.

Study or subgroup	HP paint-on N	HP paint-on Mean(SD)	HP strip N	HP strip Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
19.3.1 5.9% HP paint-on versus 5.9% HP strip							
Auschill 2007	20	-4 (2.2)	20	-3.7 (3)		100%	-0.25[-1.88,1.38]
Subtotal ***	**20**		**20**			**100%**	**-0.25[-1.88,1.38]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.3(P=0.76)							

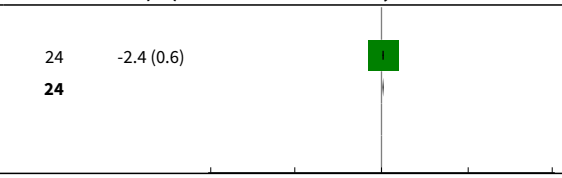


Comparison 20. SPC paint-on versus HP strip

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 19% SPC paint-on versus 6% HP strip - 6 months	1	47	Mean Difference (IV, Random, 95% CI)	0.93 [0.59, 1.27]

Analysis 20.1. Comparison 20 SPC paint-on versus HP strip, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	SPC paint-on N	SPC paint-on Mean(SD)	HP strip N	HP strip Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
20.1.1 19% SPC paint-on versus 6% HP strip - 6 months							
Bizhang 2007	23	-1.5 (0.6)	24	-2.4 (0.6)		100%	0.93[0.59,1.27]
Subtotal ***	**23**		**24**			**100%**	**0.93[0.59,1.27]**
Heterogeneity: Not applicable							
Test for overall effect: Z=5.36(P<0.0001)							

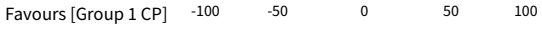


Comparison 21. CP paint-on versus CP paint-on

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 18% CP 2x versus 18% CP 4x - 1 week	1	69	Mean Difference (IV, Random, 95% CI)	1.39 [0.50, 2.28]
1.2 18% CP versus 16.4% CP - 2 weeks	1	93	Mean Difference (IV, Random, 95% CI)	-0.70 [-2.21, 0.81]

Analysis 21.1. Comparison 21 CP paint-on versus CP paint-on, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	Group 1 CP N	Group 1 CP Mean(SD)	Group 2 CP N	Group 2 CP Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
21.1.1 18% CP 2x versus 18% CP 4x - 1 week							
Li 2004	35	-2.8 (2.3)	34	-4.2 (1.3)		100%	1.39[0.5,2.28]
Subtotal ***	**35**		**34**			**100%**	**1.39[0.5,2.28]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.08(P=0)							
21.1.2 18% CP versus 16.4% CP - 2 weeks							
Brunton 2004	46	8.2 (3.4)	47	8.9 (4)		100%	-0.7[-2.21,0.81]
Subtotal ***	**46**		**47**			**100%**	**-0.7[-2.21,0.81]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.91(P=0.36)							
Test for subgroup differences: Chi^2=5.49, df=1 (P=0.02), I^2=81.78%							

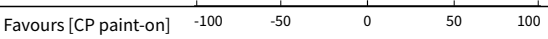


Comparison 22. CP paint-on versus HP paint-on

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 25% CP paint-on versus 8.75% HP paint-on	1	59	Mean Difference (IV, Random, 95% CI)	-0.16 [-1.39, 1.07]

Analysis 22.1. Comparison 22 CP paint-on versus HP paint-on, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	CP paint-on N	CP paint-on Mean(SD)	HP paint-on N	HP paint-on Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.1.1 25% CP paint-on versus 8.75% HP paint-on							
Nathoo 2003	30	6.5 (2.2)	29	6.7 (2.6)		100%	-0.16[-1.39,1.07]
Subtotal ***	**30**		**29**			**100%**	**-0.16[-1.39,1.07]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.25(P=0.8)							



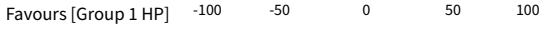
Comparison 23. HP paint-on versus HP paint-on

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 6% HP paint-on versus 6% HP + KF paint-on	1	67	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.56, 0.36]

Analysis 23.1. Comparison 23 HP paint-on versus HP paint-on, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	Group 1 HP N	Group 1 HP Mean(SD)	Group 2 HP N	Group 2 HP Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
23.1.1 6% HP paint-on versus 6% HP + KF paint-on							
Ziebolz 2008	33	2.7 (1)	34	2.8 (0.9)		100%	-0.1[-0.56,0.36]
Subtotal ***	**33**		**34**			**100%**	**-0.1[-0.56,0.36]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.43(P=0.67)							

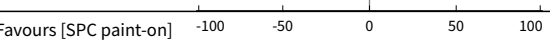


Comparison 24. SPC paint-on versus CP paint-on

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 19% SPC paint-on versus 18% CP paint-on - 14 days	1	38	Mean Difference (IV, Random, 95% CI)	-0.58 [-0.95, -0.21]

Analysis 24.1. Comparison 24 SPC paint-on versus CP paint-on, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	SPC paint-on N	SPC paint-on Mean(SD)	CP paint-on N	CP paint-on Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
24.1.1 19% SPC paint-on versus 18% CP paint-on - 14 days							
Barlow 2003	19	-1.1 (0.6)	19	-0.5 (0.6)		100%	-0.58[-0.95,-0.21]
Subtotal ***	**19**		**19**			**100%**	**-0.58[-0.95,-0.21]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.06(P=0)							

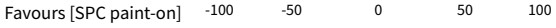


Comparison 25. SPC paint-on versus HP paint-on

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Tooth whitening - assessed by the dentist	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 19% SPC paint-on versus 8.7% HP paint-on	1	56	Mean Difference (IV, Random, 95% CI)	-0.36 [-0.71, -0.01]

Analysis 25.1. Comparison 25 SPC paint-on versus HP paint-on, Outcome 1 Tooth whitening - assessed by the dentist.

Study or subgroup	SPC paint-on N	SPC paint-on Mean(SD)	HP paint-on N	HP paint-on Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
25.1.1 19% SPC paint-on versus 8.7% HP paint-on							
Gerlach 2003	29	-0.6 (0.7)	27	-0.2 (0.7)		100%	-0.36[-0.71,-0.01]
Subtotal ***	**29**		**27**			**100%**	**-0.36[-0.71,-0.01]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.01(P=0.04)							



ADDITIONAL TABLES

Table 1. Details of analyses performed in multiarm trials

Trial	Interventions reported in the trials	Interventions considered in analyses	Reason
Aka 2017	• Placebo • 10% carbamide peroxide (Opalescence PF) gel in tray • 6% hydrogen peroxide (Opalescence Go) gel in tray	Bleaching agent vs placebo • 10% carbamide peroxide gel in tray vs placebo Bleaching agent vs bleaching agent • 10% carbamide peroxide gel in tray vs 6% hydrogen peroxide gel in tray	Most commonly used concentrations
Alonso 2014	• 10% carbamide peroxide in tray • 15% carbamide peroxide in tray • 7.5% hydrogen peroxide in tray • 9.5% hydrogen peroxide in tray	Bleaching agent vs bleaching agent • 10% carbamide peroxide in tray vs 7.5% hydrogen peroxide in tray	Most commonly used concentrations
Bizhang 2007	• 6% hydrogen peroxide whitening strips • 19% sodium percarbonate brush-applied gel that dries to a film • Placebo brush-applied gel without peroxide	Bleaching agent vs placebo • 6% hydrogen peroxide whitening strips vs placebo Bleaching agent vs bleaching agent	Most commonly used concentrations

Table 1. Details of analyses performed in multiarm trials *(Continued)*

		• 19% sodium percarbonate brush-applied gel that dries to a film vs 6% hydrogen peroxide whitening strips	
Browning 2008	• 10% carbamide peroxide in tray • 10% carbamide peroxide, 3% potassium nitrate in tray • 10% carbamide peroxide, 0.5% potassium nitrate in tray • 10% carbamide peroxide, 0.5% potassium nitrate, 0.25% sodium fluoride in tray • Placebo	Bleaching agent vs placebo • 10% carbamide peroxide, 0.5% potassium nitrate, 0.25% sodium fluoride in tray vs placebo Bleaching agent vs bleaching agent • 10% carbamide peroxide in tray vs 10% carbamide peroxide, 0.5% potassium nitrate, 0.25% sodium fluoride in tray	Most commonly used concentrations
Gerlach 2000	• 5.3% hydrogen peroxide strips • 10% carbamide peroxide gel in tray • 15% carbamide peroxide gel in tray • 20% carbamide peroxide gel in tray	Bleaching agent vs bleaching agent • 5.3% hydrogen peroxide strips vs 10% carbamide peroxide gel in tray	Most commonly used concentrations
Hyland 2015	• 5% carbamide peroxide gel • 10% carbamide peroxide gel • Placebo	Bleaching agent vs placebo • 5% carbamide peroxide gel vs placebo Bleaching agent vs bleaching agent • 5% carbamide peroxide gel vs 10% carbamide peroxide gel	Most commonly used concentrations
Krause 2008	• 10% carbamide peroxide gel in tray • 17% carbamide peroxide gel in tray • 0% carbamide peroxide gel in tray (control)	Bleaching agent vs bleaching agent • 10% carbamide peroxide gel in tray vs 17% carbamide peroxide gel in tray	Most commonly used concentrations
Li 2003	• 6.5% hydrogen peroxide strips • 7.5% hydrogen peroxide gel in tray • 16% carbamide peroxide gel in tray	Bleaching agent vs bleaching agent • 6.5% hydrogen peroxide strips vs 16% carbamide peroxide gel in tray	Most commonly used concentrations
Li 2004	• 18% carbamide peroxide 2x paint-on gel • 18% carbamide peroxide 3x paint-on gel • 18% carbamide peroxide 4x paint-on gel	Bleaching agent vs bleaching agent • 18% carbamide peroxide 2x paint-on gel vs 18% carbamide peroxide 4x paint-on gel	Most commonly used concentrations
Matis 2006	• 10% carbamide peroxide gel in tray • 15% carbamide peroxide gel in tray • 20% carbamide peroxide gel in tray	Bleaching agent vs bleaching agent • 10% carbamide peroxide gel in tray vs 15% carbamide peroxide gel in tray	Most commonly used concentrations
Wong 2004	• 6% hydrogen peroxide strips • 18% carbamide peroxide paint-on gel • Placebo: non-whitening toothpaste	Bleaching vs placebo • 6% hydrogen peroxide strips vs placebo Bleaching agent vs bleaching agent • 6% hydrogen peroxide strips vs 18% carbamide peroxide paint-on gel	Most commonly used concentrations

Table 1. Details of analyses performed in multiarm trials *(Continued)*

Xu 2007	• 6% hydrogen peroxide strips • 5.8% hydrogen peroxide paint-on gel • Placebo: negative control (water rinse)	Bleaching vs placebo • 6% hydrogen peroxide strips vs placebo Bleaching agent vs bleaching agent • 5.8% hydrogen peroxide paint-on gel vs 6% hydrogen peroxide strips	Most commonly used concentrations

vs = versus; 2x = twice; 3x = 3 times; 4x = 4 times.

Table 2. Comparison of included articles: 2006 review version versus current version

The 2006 review included 25 trials of which 17 trials were included in our review, 3 are under awaiting classification, 2 articles were excluded with reason, 2 were discarded during the initial screening, and 1 did not appear in our search and we could not obtain a copy of:

2006 review	Current review		
Included records	**Included records**	**Awaiting classification**	**No longer included**
Barnes 1998 Brunton 2004 Cronin 2005 Gerlach 2000 Gerlach 2001 Gerlach 2002 Gerlach 2002a Gerlach 2003 Gerlach 2004a Gerlach 2004b Karpinia 2002 Karpinia 2003 Kihn 2000 Kowitz 1994 Kowitz 1994a Kugel 2000 Li 2003 Li 2004 Matis 2000 Mokhlis 2000 Nathoo 1994	Brunton 2004 Cronin 2005 Gerlach 2000 Gerlach 2002 Gerlach 2002a Gerlach 2003 Karpinia 2002 Kihn 2000 Kowitz 1994 Kugel 2000 Li 2003 Li 2004 Matis 2000 Mokhlis 2000 Nathoo 1994 Nathoo 2002 Nathoo 2003	Barnes 1998: unclear if the trial is a randomised controlled trial Gerlach 2004b: full-text not available Sielski 2003: full-text not available (We did not use the data from the previous review as we needed to be sure about the studies characteristics)	Gerlach 2001: reported on an anticavity whitening dentifrice; discarded during initial screening Gerlach 2004a: 1 of the interventions included a whitening dentifrice; excluded with reason Karpinia 2003: 1 of the interventions included a whitening dentifrice; excluded with reason Kowitz 1994a: reported on whitening toothpaste; discarded during initial screening Panich 2001: an MSc thesis, did not appear in our search. We could neither procure the full text of the thesis nor the published version, hence we did not include in our review

Table 2. Comparison of included articles: 2006 review version versus current version *(Continued)*

Nathoo 2002
Nathoo 2003
Panich 2001
Sielski 2003

APPENDICES

Appendix 1. Cochrane Oral Health's Trials Register search strategy

1 (((tooth or teeth or dental) and (whiten* or bleach*)):ti,ab) AND (INREGISTER)
2 (((tooth or teeth or dental) and (stain* and remov*)):ti,ab) AND (INREGISTER)
3 (#1 or #2) AND (INREGISTER)
4 (("tooth whitening system" or "tooth bleaching system"):ti,ab) AND (INREGISTER)
5 ((tray* and (whiten* or bleach* or peroxide)):ti,ab) AND (INREGISTER)
6 ((strip* or dentifrice* or gel* or toothpaste* or paste* or rins* or mouthwash* or mouthrins* or "mouth wash*" or "mouth rins*"):ti,ab) AND (INREGISTER)
7 ("whitening kit*":ti,ab) AND (INREGISTER)
8 (#4 or #5 or #6 or 7) AND (INREGISTER)
9 (#3 and #8) AND (INREGISTER)

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 [mh "tooth bleaching"]
#2 ((tooth or teeth or dental) near/5 (whiten* or bleach* or (stain* near/3 remov*))):ti,ab
#3 #1 or #2
#4 ("tooth whitening system" or "tooth bleaching system"):ti,ab
#5 (tray* and (whiten* or bleach* or peroxide)):ti,ab
#6 [mh dentifrices]
#7 ((strip* or dentifrice* or gel* or toothpaste* or paste* or rins* or mouthwash* or mouthrins* or "mouth wash*" or "mouth rins*") and (whiten* or bleach* or peroxide)):ti,ab
#8 "whitening kit*":ti,ab
#9 {or #4-#8}
#10 #3 and #9

Appendix 3. MEDLINE Ovid search strategy

1. Tooth bleaching/
2. ((tooth or teeth or dental) adj5 (whiten$ or bleach$ or (stain$ adj3 remov$))).ti,ab.
3. 1 or 2
4. ("tooth whitening system" or "tooth bleaching system").ti,ab.
5. (tray$ and (whiten$ or bleach$ or peroxide)).ti,ab.
6. Dentifrices/
7. ((strip$ or dentifrice$ or gel$ or toothpaste$ or paste$ or rins$ or mouthwash$ or mouthrins$ or "mouth wash$" or "mouth rins$") and (whiten$ or bleach$ or peroxide)).ti,ab.
8. "whitening kit$".ti,ab.
9. or/4-8
10. 3 and 9

This subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity- maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the*Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.1.0 (updated March 2011) (Lefebvre 2011).

1. randomised controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.

6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. Embase Ovid search strategy

1. tooth discoloration/
2. ((tooth or teeth or dental) adj5 (whiten$ or bleach$ or (stain$ adj3 remov$))).ti,ab.
3. 1 or 2
4. tooth bleaching agent/
5. ("tooth whitening system" or "tooth bleaching system").ti,ab.
6. (tray$ and (whiten$ or bleach$ or peroxide)).ti,ab.
7. toothpaste/
8. (strip$ or dentifrice$ or gel$ or toothpaste$ or paste$ or rins$ or mouthwash$ or mouthrins$ or "mouth wash$" or "mouth rins$").ti,ab.
9. "whitening kit$".ti,ab.
10. or/4-9
11. 3 and 10

This subject search was linked to an adapted version of the Cochrane Embase Project filter for identifying randomised controlled trials in Embase Ovid (see http://www.cochranelibrary.com/help/central-creation-details.html for information).

1. Randomized controlled trial/
2. Controlled clinical study/
3. Random$.ti,ab.
4. randomization/
5. intermethod comparison/
6. placebo.ti,ab.
7. (compare or compared or comparison).ti.
8. ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
9. (open adj label).ti,ab.
10. ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
11. double blind procedure/
12. parallel group$1.ti,ab.
13. (crossover or cross over).ti,ab.
14. ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant $1)).ti,ab.
15. (assigned or allocated).ti,ab.
16. (controlled adj7 (study or design or trial)).ti,ab.
17. (volunteer or volunteers).ti,ab.
18. trial.ti.
19. or/1-18
20. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
21. 19 not 20

Appendix 5. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov search strategy

whiten and teeth
bleach and teeth
tooth and stain and removal

Appendix 6. World Health Organization International Clinical Trials Registry Platform search strategy

whiten and tooth or whiten and teeth
bleach and tooth or bleach and teeth
tooth and stain and removal

WHAT'S NEW

Date	Event	Description
12 June 2018	New citation required and conclusions have changed	New authors. Review update including 46 new studies bringing the total to 71 included studies. Methods updated. 'Summary of findings' tables included. Conclusions changed.
12 June 2018	New search has been performed	Searches updated to 12 June 2018.

CONTRIBUTIONS OF AUTHORS

- Prashanti Eachempati: protocol, selecting trials, analyses, final review, and updating review.
- Sumanth Kumbargere Nagraj: arbiter, analyses, final review, and updating review.
- Salian Kiran Kumar Krishanappa: obtaining copies of trials, selecting trials, data extraction, and entering data into Review Manager 5.
- Puneet Gupta: selecting trials, data extraction, and entering data into Review Manager 5.
- Ibrahim Ethem Yayali: selecting trials, data extraction, and entering data into Review Manager 5.

DECLARATIONS OF INTEREST

Prashanti Eachempati: none known.
Sumanth Kumbargere Nagraj: none known.
Salian Kiran Kumar Krishanappa: none known.
Puneet Gupta: none known.
Ibrahim Ethem Yaylali: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are a few differences between the previous version of the review and this updated version.

- Previous review considered outcome data for tooth whiteness immediately after 2 weeks of product applications whereas we considered trials with any duration of treatment.
- This version excluded quasi-randomised trials.
- Trials addressing bleaching for tetracycline-stained teeth were not included in the previous review. We included two trials comparing the effects of a bleaching agent on participants with tetracycline stains.
- Some trials which were included in the previous review are not included in the present review as they consisted of whitening dentifrices which were part of our exclusion criteria (Additional Table 2).
- Trials on whitening chewing gums and mouthrinses are included in our current review but absent in the previous review.
- In the previous review analysis was not combined for trials with the same bleaching agent using different measurement methods (Vita shade guide and colorimeter). We used standardised mean difference (SMD) and combined data wherever relevant.

- Report on examiner calibration and correlation analysis between concentration of peroxide and effect size was not included in our review but is mentioned in the previous review.
- We updated the methods, used GRADE to assess the certainty of the evidence and included 'Summary of findings' tables.

INDEX TERMS

Medical Subject Headings (MeSH)

Carbamide Peroxide [adverse effects] [therapeutic use]; Chewing Gum; Hydrogen Peroxide [adverse effects] [therapeutic use]; Mouthwashes [therapeutic use]; Nonprescription Drugs; Phosphates [therapeutic use]; Polyphosphates [therapeutic use]; Randomized Controlled Trials as Topic; Self Care [*methods]; Tooth Bleaching [adverse effects] [*methods]; Tooth Bleaching Agents [adverse effects] [*therapeutic use]; Toothpastes [therapeutic use]; Urea [therapeutic use]

MeSH check words

Adult; Humans